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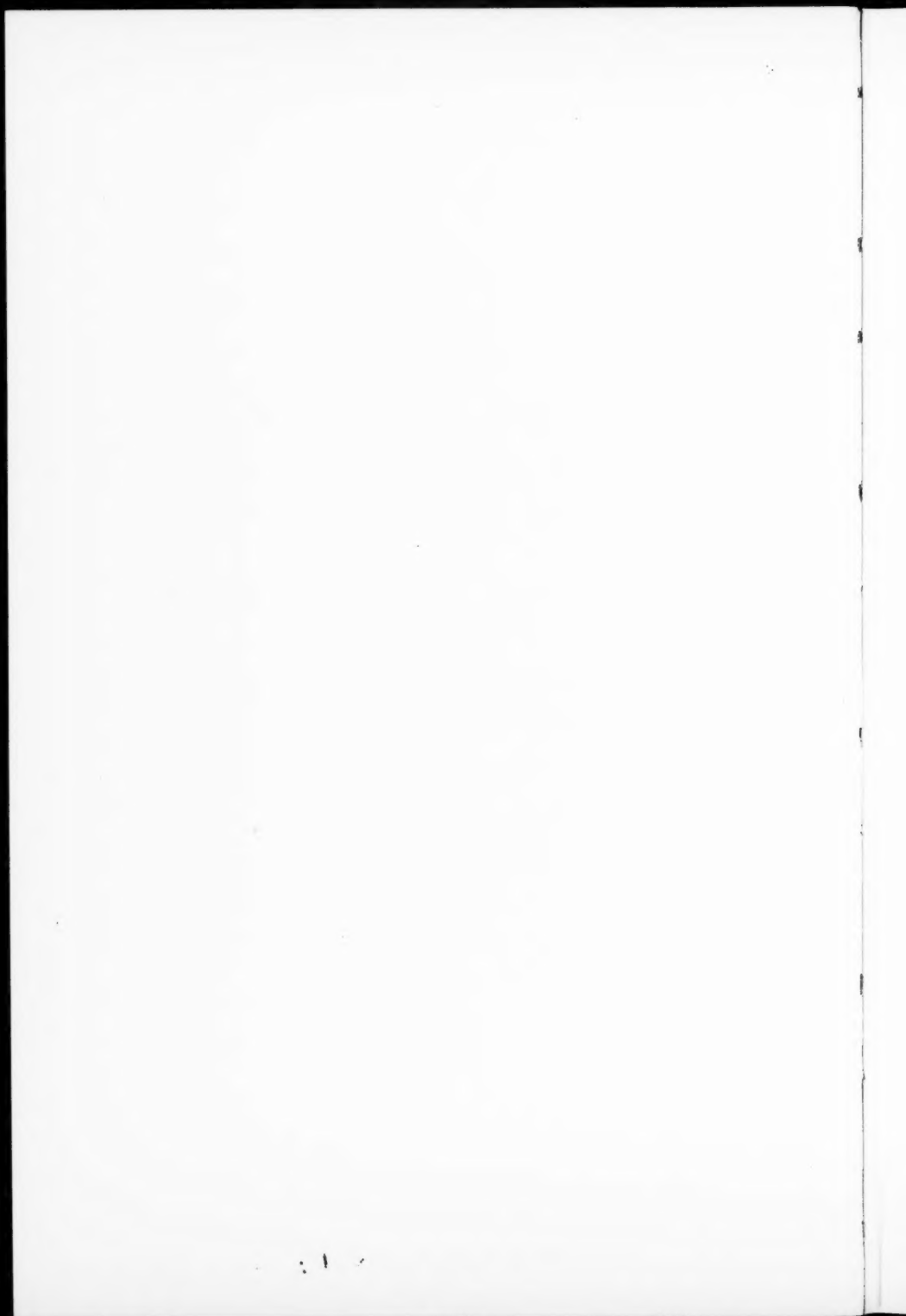
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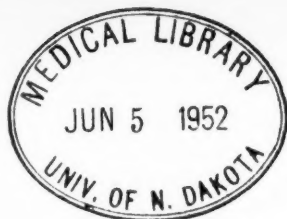
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THE MEDICAL CLINICS OF NORTH AMERICA

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No. 3

CONTRIBUTION BY DR. HERMAN O. MOSENTHAL

NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL

THE INTERPRETATION OF SUGAR TOLERANCE TESTS. THE COMMON OCCURRENCE OF RENAL GLYCOSURIA

THE present figures and facts were collected to determine the value of sugar tolerance tests in interpreting the significance of casual traces of sugar in the urine. Reports are frequently made of intermittent glycosuria, especially during life insurance examinations, which may or may not be due to diabetes. Often after many urinary analyses and occasional blood-sugar estimations the problem is no nearer solution than it was at the beginning, and final recourse is had to sugar tolerance tests. The diagnostic results obtained from these have not been satisfactory; the attempt will be made to clear up this situation as far as possible.

Method of Procedure.—It is generally agreed that the sugar tolerance test should be carried out in the morning before the patient has received any breakfast. Sometimes a small amount of food is allowed; apparently this makes very little difference. The test material is nearly always glucose; various doses have been recommended; about the same results are obtained whether the glucose is given so many grams per kilo or in set amounts of 50 to 100 grams, or more or less; the idea of giving the glucose according to body weight entails a great amount of detail that appears to be unnecessary, especially as heavy persons contain no more muscular and glandular tissues than thin individuals, but have only more fat, that has no influence on the metabolism

of glucose so far as this test is concerned. One hundred grams is the amount of glucose generally used; this may be accepted as the most convenient standard and the one with which more data are available for comparative study than with any other. In order to avoid nausea the glucose is preferably administered dissolved in about $1\frac{1}{2}$ tumblerfuls of water and served ice cold; water may be taken frequently during the test. The intervals at which blood-sugar determinations and urine analyses are made, after the sugar solution is swallowed, vary a good deal according to the data that are desired. What might be termed a "complete sugar tolerance test" entails the following:

(1) A fasting blood-sugar and urine analysis for glucose; this furnishes *data concerning the carbohydrate metabolism when there is least strain put upon it.*

(2) Blood-sugar and urinary examinations twenty, forty, and sixty minutes after the ingestion of glucose; this enables us to draw conclusions as to:

(a) The *maximal blood-sugar value reached*; this occurs normally in forty-five minutes more or less.

(b) The renal threshold to glucose; cases of glycosuria of doubtful significance are frequently instances of *renal glycosuria* and not diabetes, and in our experience this has been a very important aspect of the situation, if all diagnostic justice is to be accorded these cases.

(3) Blood-sugar and urinary analysis at the end of two hours, to determine the *duration of the blood curve* and obtain possible further data on the renal threshold.

To Summarize.—In carrying out a "complete" sugar tolerance test the fasting subject is given 100 grams of glucose in solution served ice cold; glucose determinations are made on the blood and urine before the ingestion of glucose and at twenty, forty, sixty, and one hundred and twenty minute intervals afterward. The procedure may be simplified if the examiner desires to develop only a limited number of points instead of the full information that sugar tolerance tests will yield.

In studying this problem it has been found convenient and very helpful to consider the *facts that have been stressed as the*

crucial ones in interpreting sugar tolerance tests and then value them in the best possible way. They may be regarded as:

- (1) The fasting blood-sugar level.
- (2) The maximal value of blood-sugar attained.
- (3) The duration of the blood-sugar curve, that is, the time required for the blood-sugar to reach normal after the glucose ingestion has resulted in a rise in the blood-sugar.
- (4) The renal threshold for glucose; in other words, the problem of renal glycosuria.

The Fasting Blood-sugar Level.—This has been determined innumerable times by very many observers. It may serve to make a long story short to give the figures arrived at by Gray in summarizing this subject. He collected fasting blood-sugar determinations in 431 persons clinically normal; in all of them the blood-sugar was 120 mg. per 100 c.c. or less, except in 10; in 8 of these it was 130, in 1, 150, and in 1, 160. Taking into consideration that there may have been some errors in technic and that some of these subjects may have not been absolutely normal it seems only proper to disregard the small number of results higher than 120 and to consider *120 mg. of glucose per 100 c.c. of blood as the upper normal limit for sugar in the blood of the fasting human being.* Some authors, as Gray, consider the fasting blood-sugar one of the most important if not the most important point in the sugar tolerance test. It is evident that higher than normal fasting glycemia must signify a lowered sugar tolerance; however, it must be borne in mind, as will be elaborated further on, that not every case of diminished carbohydrate tolerance has diabetes mellitus, nor does every instance of lowered sugar tolerance have an increased fasting blood-sugar. However, in interpreting blood-sugar curves none of them have been considered in the present paper as normal unless their fasting blood-sugar has been 120 mg. per 100 c.c. or less.

The Maximal Value of Blood-sugar After the Indigestion of 100 Gms. of Glucose.—Very great difference of opinion prevails in regard to this figure; in fact, this statement may be applied to all points concerning blood-sugar curves except the fasting blood-sugar level which has been discussed in the previous paragraph.

It is only necessary to glance at the summary of 300 blood-sugar curves as given by Gray (Table 1) to realize what a wide

TABLE 1
Summary of compilation of 300 blood-sugar curves of normal persons (Gray).

Blood-sugar mg. per 100 c.c.					
	Fasting.	After glucose.			
		One-half hour.	One hour.	Two hours.	Three hours.
Lowest.....	40	60	40	30	40
Highest.....	160	230	280	260	170
	8 above	1 above	2 above	1 above
	120	240	160	140
Mean.....	90	140	120	110	90
Mode.....	100	140	110	100	80
Per cent. above					
160.....	0	20	13	1	1

variation may occur. If all the normal values are to be included it is obvious that most of the curves which indicate a diminished sugar tolerance must be classed among the normals; this would defeat our immediate object of setting up a normal standard. A ray of light is possibly shed on the situation when the last line of the table giving the per cent. of values above 160 mg. of blood-sugar per 100 c.c. is studied. Except at the half- and one-hour intervals 160 mg. certainly would indicate the upper normal limit. Many authors have considered this as the upper normal limit throughout the curve. This is the case in Tables 2 and 3.

On the other hand, there are many examples among normal individuals in which the maximal blood-sugar level rises distinctly above 160 (Tables 4 and 5). This is undoubtedly correct.

We have nevertheless decided to accept 160 mg. per 100 c.c. as the highest normal blood-sugar value that should be obtained after the taking of 100 gm. of glucose. It is only claimed that this conclusion is arrived at from both a practical study of the problem and a survey of the literature. It must largely re-

TABLE 2

Blood-sugar curves of six normal individuals according to Hamman and Hirschman.

Blood-sugar mg. per 100 c.c.		Minutes after glucose, highest blood-sugar.	Duration blood-sugar curve, minutes.	Type blood-sugar curve.
Fasting.	Highest.			
96	138	21	38	Normal.
91	148	20	45	Normal.
96	124	105	120	Normal.
101	137	45	60	Normal.
90	124	30	60	Normal.
79	87	45	60	Low.

TABLE 3

Blood-sugar curves of six normal persons published by Pemberton and Foster.

Blood-sugar mg. per 100 c.c.		Minutes after glucose highest blood-sugar.	Duration blood-sugar curve, minutes.	Type blood-sugar curve.
Fasting.	Highest.			
108	122	60	120	Normal.
104	138	30	60	Normal.
101	147	30	120	Normal.
111	158	30	60	Normal.
128	138	30	60	Normal.
97	122	30	60	Normal.

TABLE 4

Normal blood-sugar curves of Linder, Hiller, and Van Slyke; none of them are absolutely within the present "normal."

Blood-sugar mg. per 100 c.c.		Minutes after glucose highest blood-sugar.	Duration blood-sugar curve, minutes.	Type blood-sugar curve.
Fasting.	Highest.			
91	140	30	150	Slightly prolonged.
94	147	30	180	Slightly prolonged.
92	157	30	200	Prolonged.
73	164	30	150	High prolonged.
89	194	30	100	High.
97	200	30	180	High prolonged.

TABLE 5

Normal blood-sugar curves according to Maclean; he terms these "lag curves"; they have been termed "high curves" in this presentation.

Blood-sugar mg. per 100 c.c.		Minutes after glucose highest blood-sugar.	Duration blood-sugar curve, minutes.
Fasting.	Highest.		
90	174	45	90
100	164	30	60
102	173	60	120
104	224	30	90
102	205	30	120
125	212	30	90
118	216	30	120
116	205	30	90
96	196	30	120

main a question of personal impressions. What should be distinctly understood is that a blood-sugar above 160 mg. during a sugar tolerance test does not necessarily indicate diabetes, but only serves to show that there is an impairment of the body's ability to metabolize glucose, which may be found in many conditions besides diabetes and even in so-called normal persons.

The Duration of the Blood-sugar Curve.—Maclean says: "The ability to get rid of the increased blood-sugar and to return to a normal blood-sugar value within a limited time after a sugar test is undoubtedly the best indication of an effective carbohydrate metabolism." It is interesting to note that here we have a second opinion as to what constitutes the most valuable point in a blood-sugar curve. What is the normal duration of a blood-sugar curve? This is an extremely difficult question to answer largely because of the lack of concordant results. In the first place, we have regarded a blood-sugar as returning to normal when it reaches the level of 120 mg. per 100 c.c. of blood. In the second place, the time required to accomplish this has been generally believed to be less than two hours (Tables 2 and 3), though some authors (as in Table 4) believe the period to be longer. We have adopted the conservative attitude of

considering one hundred and twenty minutes as the normal limit for the duration of the blood-sugar curve.

Types of Blood-sugar Curves.—With the above normal criteria in mind we are now in a position to “classify” blood-sugar curves. The types suggested are a good deal similar to those offered as Types 1, 2, and 3 by McCasky, and Rohdenburg, Bernhard, and Krehbiel, but have the double advantage of resting on a more definite standard of figures and having designations that describe the type of curve, thus being easier to remember and employ in diagnostic readings. (See Table 6.)

TABLE 6

Proposed standards for blood-sugar curves. Test dose is 100 gm. of glucose.

Types of curve.	Blood-sugar mg. per 100 c.c.		Duration ¹ curve, minutes.	Significance.
	Fasting.	Highest.		
Normal.....	120—	120+ 160—	120—	Normal sugar tolerance.
High.....	120±	161+	120—	Diminished sugar tolerance.
Prolonged.....	120—	160—	121+	Diminished sugar tolerance.
High prolonged...	120±	161+	121+	Diminished sugar tolerance.
Low.....	120—	120—	0	Increased sugar tolerance.

The standards given in this table (Table 6) are based on the ideas previously elaborated, that the normal fasting blood-sugar should be 120 mg. or less, that after the administration of 100 gm. of glucose the blood-sugar should not rise above 160 and that the blood-sugar should return to 120 mg. or less within two hours; any curve in which the blood-sugar rises above 160 mg. has been termed a “high curve”; any curve which lasts longer than two hours has been designated as “prolonged.” There remain the so-called “low curves” to be considered.

Those curves are regarded as “low” in which at no time during the period of observation the blood-sugar rises above 120 mg. per 100 c.c. Cummings and Piness (Table 7) furnish many

¹ The curve is considered to terminate when the blood-sugar returns to a level of 120 mg.

examples of this sort. Such low curves exist in normals, as found by other authors as well (Table 9), and in pathologic conditions

TABLE 7

Examples of "low curves," from Cummings and Piness, obtained in normal individuals.

Blood-sugar mg. per 100 c.c.		
Fasting.	One hour.	Two hours.
37	38	62
44	73	77
46	63	56
49	101	68
50	114	97
52	71	68
52	71	68
55	92	71
55	89	95

are helpful in diagnosis, as in the hypopituitary patient cited in Table 8.

TABLE 8

Example of a "low" blood-sugar curve, indicating an increased sugar tolerance, in a case of hypopituitarism.

Blood-sugar mg. per 100 c.c.	Remarks.
81.....	Fasting, 100 gm. glucose
109.....	One hour after glucose
91.....	Two hours after glucose

It may have been noted in the quotations given from each group of observers that the limits of the normal variations coincide very closely within their own series, but that one set of figures does not necessarily bear much resemblance to the others. This is extremely interesting and would seem to be perplexing if we are to value the reports as indicating the limits of normal variations. The explanation which offers itself as the most likely one is that the normals of each group have certain characteristics: age, occupation, dietary habits, etc., in common

that may lend a uniformity to their carbohydrate metabolism. From the articles quoted it would appear that medical students, older laboratory workers, soldiers, and ward, dispensary, or private patients were variously resorted to as the normal material. None of the series thus far alluded to is very large; when a greater number of normal persons is examined, as was done by Goto and Kuno, it becomes evident that every one of the possible types of blood-sugar curves mentioned in Table 6 will be represented (Table 9). From all these facts it may be

TABLE 9
Types of "sugar curves" found among 53 normal individuals tested by Goto and Kuno.

Blood-sugar mg. per 100 c.c.					Duration, minutes.	Type blood-sugar curve.
Fasting.	Highest.		Two hours.	Three hours.		
	Milli- grams.	In min- utes.				
109	153	40	127	131	180+	"Prolonged."
116	185	90	147	135	180+	
114	163	60	126	134	180+	
109	231	40	204	195	180+	"High prolonged."
104	206	60	132	119	180	
94	230	60	147	173	180+	
88	160	40	93	76	90	"Normal."
96	147	20	99	101	90	
96	155	60	101	118	120	
91	114	180	86	114	?	"Low."
89	117	40	109	92	?	
79	118	40	84	72	?	

concluded that there are many so-called normal persons who have blood-sugar curves that indicate either a diminished or an increased tolerance for glucose.

The proper valuation of these findings demands a revision of the ideas concerning the relation of glucose tolerance to diabetes that have been more or less generally subscribed to.

It has been thought that an impaired carbohydrate metabolism and diabetes were synonymous; subsequently knowledge was acquired which showed that there were many pathologic conditions (thyroid disturbances, nephritis, thrombo-angiitis obliterans, etc.) in which the blood-sugar curves after glucose administration were apparently identical with those obtained in cases of diabetes mellitus, and the statement has often been made that in these conditions, especially in arteriosclerosis, a latent diabetes mellitus exists. If we include in our clinical definition of diabetes mellitus the idea that diabetes is a disease characterized by a progressive diminution of carbohydrate tolerance, it becomes evident, inasmuch as scarcely any cases of arthritis, arteriosclerosis, nephritis, etc., develop a persistent and constantly increasing glycosuria, that these patients are not prediabetic and, furthermore, which is most important, every instance of diminished sugar tolerance does not point to diabetes mellitus.

It is impossible to explain this wide-spread occurrence of diminished carbohydrate tolerance simply by associating it on clinical grounds with this or that disease; the reasons for an impaired ability to maintain a low blood-sugar under stress must be sought for in the functional disturbance of various organs and processes in the body concerning which we have comparatively little information.

It is a justifiable belief that the severity of diabetes mellitus is directly proportional to the functional and anatomic damage of the islands of Langerhans in the pancreas. It has been shown, especially by Admont Clarke, that in the catabolism of sugar this internal secretion must be aided by other factors thus far not clearly defined. If this phase of the problem represents the combustion of sugar, we have an equally important aspect of the situation to consider in the storage of glucose as glycogen in the liver and other tissues. Differentiating between these two component factors concerned in carbohydrate metabolism, Linder, Hiller, and Van Slyke were recently able to determine that in nephritis the abnormal blood-sugar curves were due to changes in the liver and not associated with a lessened

utilization of glucose. This is a distinct step forward, and when carried out for other diseases will broaden our knowledge in regard to carbohydrate metabolism in a very useful way.

It has been very effectively proved by Mann and his associates that the liver plays a very significant rôle in controlling the blood-sugar; if the liver is extirpated the glucose content of the blood diminishes very rapidly and death follows, the course of events being materially delayed by infusions of glucose. When we consider still further that the adrenal, thyroid, and pituitary glands, the central and sympathetic nervous systems, asphyxia, certain poisons, as morphin or ether, all may influence the blood-sugar level, it becomes apparent that the number of combinations that may control glycemia are almost without number. It is of the greatest importance from the clinician's point of view to ferret out a particular process characteristic of the diminished sugar tolerance in diabetes and utilize this in the diagnosis of this malady.

Dr. John Kilian, in charge of our chemical department, has some recent results which lead us to believe that such a procedure may be achieved shortly. Meanwhile it is necessary to make the greatest possible use of the test we possess.

In a number of diseases glucose tolerance yields blood-sugar curves which are a counterpart of those found in diabetes. In order to make our interpretation of this subject as complete as possible I wish to allude to some of the results that have been obtained in a variety of conditions.

Arthritis.—All types of blood-sugar curves apparently may be elicited in arthritis (Table 10); however, the high prolonged reactions usually considered especially characteristic of a diminished sugar tolerance predominate. According to the authors quoted there was no suspicion of diabetes mellitus in any of their cases.

Hyperthyroidism.—Here again every type of blood-sugar curve is represented; the high prolonged variety is most frequently found. Even from the few cases cited it becomes apparent that the glycemic reaction and the basal metabolic rate are not proportional to one another. A satisfactory explanation

TABLE 10

Blood-sugar curves in arthritis from the series of Pemberton and Foster and of Fletcher. The high prolonged curves predominate in their findings.

Blood-sugar mg. per 100 c.c.		Duration curve, minutes.	Type of curve.
Fasting.	Highest.		
107	130	60	Normal.
94	150	120	
99	187	120	High.
104	188	120	
144	221	180+	High prolonged.
93	312	180+	
125	152	180	Prolonged.
93	146	180	
85	98	?	Low.
106	118	?	

TABLE 11

Blood-sugar curves in hyperthyroidism from various sources; the high prolonged curves predominate; all types of curve are found.

Blood-sugar mg. per 100 c.c.		Duration curve, minutes.	Basal metab- olism.	Type blood-sugar curve.
Fasting.	Maximal.			
65	210	120+	+60	High prolonged.
94	233	120+	+24	High prolonged.
120	140	120+	+31	Prolonged.
105	137	180	+36	Prolonged.
84	194	120	+22	High.
91	200	120	+47	High.
70	115	?	Low.
91	90	?	+42	Low.
95	160	120	+27	Normal.
112	153	120	+34	Normal.

of these variations from the normal in patients suffering with hyperthyroidism is lacking. The fasting blood-sugar in this disease is almost invariably within normal limits.

Nephritis.—Of the comparatively few sugar tolerance tests

TABLE 12

Examples of blood-sugar curves in nephritis; of 35 curves collected only one was not "prolonged" or "high prolonged"; this is the "low curve" shown below; in only 8 cases was the fasting blood-sugar above 120.

Blood-sugar mg. per 100 c.c.		Duration curve, minutes.	Type curve.
Fasting.	Highest.		
93	245	240	High prolonged.
95	220	210+	High prolonged.
107	227	240+	High prolonged.
74	148	180+	Prolonged.
88	153	240	Prolonged.
98	138	190	Prolonged.
100	116	?	Low.

on record in cases of nephritis practically all are prolonged or high prolonged.

Thrombo-angiitis Obliterans (Table 13).—These cases have a distinctly abnormal response to the sugar tolerance test, though all types of curve are represented.

TABLE 13

Blood-sugar curves in thrombo-angiitis obliterans. Most of these curves are "high prolonged," though there are numerous exceptions. (Strouse and Rohdenburg, Bernhard, and Krehbiel.)

Blood-sugar mg. per 100 c.c.		Duration, minutes.	Type of curve.
Fasting.	Highest.		
108	280	120++	High prolonged.
112	230	120++	High prolonged.
110	189	120	High.
100	174	120	High.
106	116	?	Low.
96	108	?	Low.
96	159	120	Normal.
99	138	120	Normal.

Gastro-intestinal Carcinoma.—Among these patients (Table 14) there are very few giving normal sugar tolerance tests. In

TABLE 14

Nearly all curves in gastro-intestinal carcinoma are high and prolonged; according to Friedenwald and Grove the fasting blood-sugar is nearly always above normal; according to Rohdenburg, Bernhard, and Krehbiel the fasting blood-sugar often is normal.

Blood-sugar mg. per 100 c.c.		Duration curve, minutes.	Type blood-sugar curve.
Fasting.	Maximal.		
106	275	120+	High prolonged.
108	288	120+	High prolonged.
114	272	120+	High prolonged.
98	160	120	Normal.
82	170	120	High.
120	167	120	High.

fact, the common occurrence of high prolonged curves has been suggested as a proper diagnostic measure in differentiating difficult cases. It would seem rather hazardous to place much dependence on the test in this connection.

Epithelioma.—Patients suffering with epithelioma (Table 15) nearly all present high prolonged curves.

TABLE 15

Blood-sugar curves from cases of epithelioma (Rohdenburg, Bernhard, and Krehbiel). There are only a few curves that are not "high prolonged."

Blood-sugar mg. per 100 c.c.		Duration curve, minutes.	Type curve.
Fasting.	Highest.		
86	249	120++	High prolonged.
100	214	120++	High prolonged.
64	187	120	High.
100	166	120	High.
95	100	?	Low.
57	100	?	Low.
105	160	120	Normal.
55	122	120	Normal.

There are undoubtedly many conditions besides those mentioned in which high prolonged blood-sugar curves may be

found. It is only necessary to recall the fact, demonstrated previously, that such curves occur among individuals considered to be normal.

Diabetes Mellitus.—If we have been interested in conditions that may yield high prolonged curves which simulate those obtained in diabetes, our attention must now be centered on the problem of whether normal curves may occur with any degree of frequency in this disease. It becomes obvious with the long list of examples of non-diabetic maladies which, by their sugar tolerance tests alone could be diagnosed as diabetes, that this measure would lose its entire value in determining the existence of diabetes mellitus if every instance of this disturbance did not exhibit a high prolonged curve.

Table 16, giving the results of 40 sugar tolerance tests in diabetics whose fasting blood-sugar was normal, suggests the

TABLE 16

Glucose tolerance test in 40 diabetics whose fasting blood-sugar was normal, collected from various sources by Gray. This table suggests that cases of diabetes may have a normal sugar tolerance. Is this possible?

Blood-sugar mg. per 100 c.c.					
	Fasting.	After glucose.			
		One-half hour.	One hour.	Two hours.	Three hours.
Mean.....	90	180	200	150	100
Minimum.....	50	110	120	80	80
Maximum	110	270	400	500	140

possibility that normal curves may be obtained. On examining what is presumably the same material, which Gray culled from the literature in constructing Table 16, a series of blood-sugar curves has been collected from diabetic cases (Table 17); these have at least one figure corresponding to the curve suggested as "normal" in the present contribution. Only those observations were charted in which the test dose was 100 gm. of glucose.

TABLE 17

Blood-sugar curves in diabetes from various sources; these curves all exhibit some elements that are within normal limits. Not all of the high prolonged curves available are given; however, of the other types, all that could be connected are cited; it is remarkable how few there are.

Blood-sugar mg. per 100 c.c.		Duration blood-sugar curve, minutes.	Remarks.
Fasting.	Highest.		
90	210	195	Normal fasting level, otherwise abnormal; occurs very frequently.
91	210	192	
103	205	210	
130	160	90	Normal or "almost normal."
90	150	150	
80	140	60	
90	225	120	"High" curves, some with normal fasting blood-sugars; these are regarded as normal by some authors.
102	197	120	
150	228	120	
164	310	120	
90	160	175	"Prolonged" curve; otherwise normal; very rare.

It is a well-known fact that very many cases of diabetes exhibit a normal blood-sugar while fasting; every one appreciates this from experience with casual blood-sugar determinations during the treatment of this disease. The occurrence of a normal fasting blood-sugar therefore is of no great significance in negating the diagnosis of diabetes mellitus. It is very striking (see Table 17) how few curves it is possible to collect that are not "high prolonged."

There must be an early stage in most cases of diabetes mellitus, as in any functional disturbance, at which time the line is so finely drawn between the normal and the abnormal that a test, such as a sugar tolerance, may give doubtful or even negative results. This prediabetic period when the power to utilize carbohydrates approaches the pathologic by gradual steps, or fluctuates irregularly from normal to abnormal and vice versa, cannot yield clear-cut results with sugar tolerance tests.

The sugar tolerance test must be considered as revealing the ability of the body to care for carbohydrates and presumably is a true index of this process. It is not a means of diagnosing a disease, but measures a function. Hence, in the prediabetic stage, if there should be a temporary gain in carbohydrate tolerance, as there must be at times, the glucose curves may be normal for the moment; if such an individual should develop diabetes later on, the test is not at fault, it gave a true picture of the state of affairs at the time it was carried out.

It is rather remarkable that so few instances, as shown in Table 17, approaching the normal curve in the early instances of diabetes, can be collected from the literature. The conclusion seems warranted that *every definite case of diabetes exhibits a high prolonged curve*. It is evident from what has been previously stated that many other conditions yield similar pictures. The main value of the sugar tolerance test therefore would be that we are able to say with assurance in case of a normal test that carbohydrate tolerance is normal at the present moment and that diabetes does not exist; a high prolonged curve has to be interpreted in conjunction with other clinical signs (glycosuria, progressive loss of carbohydrate tolerance, etc.) in order to be of value in diagnosing diabetes. High curves or prolonged curves, from the evidence available, are not characteristic of diabetes.

The above statements and conclusions have been intended for practical application in clinical medicine. It may be of interest to note how they apply to actual cases in practice. Thirty-seven patients in whom traces of sugar existed in the urine at times and in whom the diagnosis of diabetes mellitus was not definitely established were examined by "complete" sugar tolerance tests; the summary of these is given in Table 18. Dr. W. W. Herrick has kindly allowed me to use some of his observations. Most of the cases, curiously enough, have been derived from two sources: first, the unexpected glycosurias discovered on life insurance examinations; second, physicians examining their own specimens.

The first point I should like to direct attention to is the fact

TABLE 18

Analysis of complete sugar curves in 37 sugar tolerance tests in cases of glycosuria of doubtful significance.

Total No.	Type of curve.	No diabetes at end of one year or more.	Diabetes developed.	Not traced, or observed less than one year.	Renal glycosuria.
16	Normal.	11	0	5	13
11	High prolonged.	3	2	6	1
2	Prolonged.	0	0	2	1
6	High.	4	0	2	3
2	Low.	1	0	1	2
37	Total,	19	2	16	20
20	Renal glycosuria.	10	0	10	

that of these cases 19 did not develop diabetes within a year or more. The presumptive evidence of the existence of diabetes has always been urged upon those who have had even traces of sugar in their urine. The present observations certainly do not bear this out, and possibly it is unfair to condemn these individuals from two points of view, first, because the refusal of life insurance is unjust; second, the nervous strain and mental suffering attendant to living under the regimen of a chronic disease is unnecessary. It should be stressed that in most persons the diagnosis of diabetes mellitus may be definitely made after the history of the case has been taken and a urinary analysis made. The cases now under discussion are those in whom these data leave the examiner in doubt; in this class apparently a great many do not develop diabetes mellitus.

The two patients who did develop diabetes exhibited a high prolonged curve; this is in accordance with the deduction previously made that this is the only type of blood-sugar curve characteristic of diabetes mellitus. There are several instances of the high and high prolonged types of observation as shown in Table 19 that apparently were not indicative of diabetes. This bears out the conclusion already presented that neither

of these curves is a pathognomonic sign of diabetes, but only serves to show that the sugar tolerance is below the ideal standard, which is not synonymous with diabetes.

TABLE 19

"High" and "high prolonged" curves in cases of transient glycosuria that did not develop signs of diabetes mellitus within a year or more.

Blood-sugar mg. per 100 c.c.			Type of curve.
Fasting.	Highest.	Two hours.	
125	250	166 (1½ hours)	High prolonged.
120	217	149	High prolonged.
125	220	111	High.
135	225	100	High.
125	181	111	High.
133	222	111	High.

In examining these instances of high and high prolonged curves that subsequently did not yield evidences of diabetes (Table 19), it is seen that the blood-sugar rises markedly, as high as 250 mg., and that the duration of the curves is not very much beyond the usual normal of two hours. These facts serve to corroborate the idea, that must have been developing in our minds as this discussion has been progressing, namely, that the duration of the blood-sugar curve is really of greater significance than any other point in this test.

A life insurance company has recently been working on this principle (McCrudden, Francis H.). Their sugar tolerance test consists of taking 100 gm. of glucose while fasting and determining the blood-sugar at the end of two hours. The duration of the curve, which appears to be the most significant feature, is determined in this very simple and easy fashion. It would seem logical to conclude that any one not having an elevated blood-sugar (*i. e.*, above 120 mg.) at the end of two hours did not have diabetes. Table 20 shows a series of individuals, who had shown glycosuria, tested in this way. Here again it is sur-

TABLE 20

"Partial" blood-sugar curve tried by a life insurance company. Its value depends upon the presumption that the blood-sugar should return to a level of 120 mg. within two hours. According to this test many of these "suspected" cases do not have diabetes. These observations are not the same as those cited in Table 18.

Case.	Blood-sugar mg per 100 c.c.	
	Fasting.	Two hours after 100 gm. glucose.
1	111	133
2	105	111
3	105	117
4	117	117
5	111	125
6	100	117
7	105	100
8	181	250
9	80	100
10	100	86
11	95	143
12	105	125
13	105	125
14	105	133
15	95	143
16	105	166

prising to note what a comparatively large number of persons reported to have had glucose in the urine appeared to be free of diabetes.

It is not my desire to create the impression that every case is easy to diagnose; the difficulties are often very great and should not be underestimated. Possibly citing the case of D. B. W. (Table 21) may be of some value in this connection. This patient, aged forty-eight, showed a glycosuria thirteen years ago; his condition has been progressing so favorably (the blood-sugar being normal after meals, while the diet is not limited except for the total restriction of sugar and sugar-containing foods) that it was considered possible that the diagnosis of diabetes had been an error. A blood-sugar curve (Table

21) showed a high prolonged curve characteristic of diabetes and other conditions; the problem of whether diabetes exists or has ever existed remains unanswered in my opinion. At

TABLE 21

Traces of sugar in urine about 1912; present (1925) blood-sugar is normal with about 130 gm. of CH in diet; problem is whether this man has diabetes or not. Blood-sugar curve indicates lowered sugar tolerance. Son has renal glycosuria.

February 12, 1923. Age forty-eight, male. D. B. W.

	Blood-sugar mg. per 100 c.c.	Urine vol., c.c.	Urine glucose.	
			Per cent.	Gm.
Fasting.....	117	124	0	0
100 gm. glucose:				
25 minutes later...	222	40	0	0
44 minutes later...	285	15	1.11	0.17
64 minutes later...	200	14	1.42	0.20
123 minutes later..	250	58	2.00	1.16

present, as in the past, this patient is checked up every one or two months, and the carbohydrate tolerance remains unchanged.

The reason for the common occurrence of sugar in the urine that is not associated with diabetes mellitus is the great prevalence of renal glycosuria. Of the 37 patients examined (Table 18), there were 20 who gave evidences of a lowered renal threshold to glucose. The generally accepted level of glucose in the blood at which sugar should appear in the urine is 170 mg. More than half of these cases suspected of diabetes had a threshold below this level. The individual whose renal threshold is low and exhibits constant traces of sugar in the urine and a blood-sugar which is never above normal is readily diagnosed as renal glycosuria; the person whose renal threshold is higher, 130 mg. or more, and consequently only shows glycosuria intermittently, presents a more difficult problem.

An example of the former is given in Table 22, of the latter in Table 23. It is interesting to note that Table 22 is a dis-

TABLE 22

Blood-sugar curve in a case of renal glycosuria with a low renal threshold; the concentration of sugar in the urine remains constant.

May 26, 1925. Age thirty-three, male. N. A. E.

	Blood-sugar mg. per 100 c.c.	Urine glucose.	
		Per cent.	Gm.
Fasting.....	100	0.25	
100 gm. glucose:			
25 minutes later...	100	0.25	0.09
60 minutes later...	95	0.28	0.07
120 minutes later...	83	0.25	0.14

tinctly "low" type of curve, the existence of which in so-called normal individuals is not commonly encountered.

TABLE 23

Renal glycosuria; renal threshold below 153 and above 135 mg. glucose per 100 c.c. of blood; normal blood-sugar curve; after the renal threshold had once been passed sugar persisted in the urine even with a blood-sugar of 111 mg. per 100 c.c.; this case had exhibited intermittent glycosuria which could not be interpreted properly without a sugar tolerance test.

May 8, 1925. Male, age thirty-one. C. B.

	Blood-sugar mg. per 100 c.c.	Urine glucose.	
		Per cent.	Gm.
Fasting.....	117	0	0
100 gm. glucose:			
25 minutes later...	135	0	0
45 minutes later...	153	0.44	0.07
68 minutes later...	111	1.33	0.24
125 minutes later...	100	0.10	0.07

The urinary sugar in cases of renal glycosuria presenting a "high" curve fluctuates very markedly; here (see Table 24) the urine analysis alone would inevitably lead to the diagnosis of diabetes, whereas it is not usual for the high type of curve to be significant of this malady.

TABLE 24

Renal glycosuria in a case of hyperthyroidism with a "high" blood-sugar curve and a low renal threshold; the concentration of sugar in the urine here fluctuates in direct proportion to the blood-sugar; from the urine analysis alone diabetes would be diagnosed, while from the blood-sugar curve this is definitely not present; contrast this with Table 22, in which the sugar curve is "low" and the concentration of the urinary sugar constant.

1925. Female, age nineteen. E. P.

	Blood-sugar mg. per 100 c.c.	Urine glucose.	
		Per cent.	Gm.
Fasting.....	93	0.26	0.24
100 gm. glucose:			
30 minutes later...	205	2.86	5.86
60 minutes later...	150	3.26	4.89
120 minutes later..	75	0.88	0.66

It is well known that if the blood-sugar has once passed the level of the renal threshold that subsequently the glycosuria is present even below the usual threshold; this is well illustrated in Table 23 in which it is shown that whereas the renal threshold was between 135 and 153 mg. of glucose per 100 c.c. of blood while the blood-sugar was rising, it was below 111 while it was returning to the fasting level. All these factors make it very necessary to carry out complete sugar tolerance on all doubtful cases of glycosuria before a final decision is rendered.

The level of the kidney threshold in these cases of renal glycosuria is about evenly distributed at the various blood-

TABLE 25

Renal threshold in 20 cases of renal glycosuria, from the present series.

Renal threshold blood-sugar mg. per 100 c.c.	Number of cases.
100.....	4
110.....	2
120.....	3
130.....	1
140.....	5
150.....	1
160.....	4

sugar values from 100 to 160 mg. (see Table 25). This observation is of considerable importance because it shows that the various degrees of depression of the renal threshold to glucose exist with about equal frequency, and that the case which has constant traces of sugar in the urine and a renal threshold of 100 mg. or less is no more common than those with a higher level, though it is more readily diagnosed unless a test such as sugar tolerance is resorted to.

Very many authors report cases of renal glycosuria that have not developed diabetes mellitus. None of the cases in this series have thus far shown any signs of the disease. Renal glycosuria from the knowledge gained thus far apparently is a harmless anomaly. There are certain cases of diabetes that at the same time have a lowered renal threshold to glucose. We have met with at least 3 such patients, 2 in children and 1 in an adult; these patients were treated before the time when insulin was available and all of them lost ground very rapidly. It would be fair to assume that renal glycosuria and diabetes are not etiologically related to each other in any way, and are two conditions of an entirely different nature, though they may exist in the same patient. Patients with renal glycosuria should receive the same consideration as normals, especially as far as life insurance is concerned.

In the present series there were 2 cases of renal glycosuria in brothers and, in addition, in 2 sisters, though a full sugar curve was not carried out in the latter. Several such instances have been reported. There is one other observation that is extremely interesting and well worth noting; this is the case of A. W. G. (Table 26), in whom it is established beyond doubt that the renal glycosuria was acquired for no apparent reason at the age of sixty-six and that in over five years subsequently the condition persisted and did not change into, or exhibit any signs of, diabetes mellitus. This patient, a physician, had for twenty years examined his urine about every two weeks with the purpose of using his specimen as a normal control test while carrying out life insurance examinations. At the end of this period glycosuria appeared. He proved to have constant traces

TABLE 26

Age sixty-six, male. A. W. G.

January 20, 1920: Two weeks ago sugar found in urine; never any sugar previous to that time; urine examined every two weeks for twenty years.

April 21, 1925: Traces of sugar persist in urine; feels well; full diet.

Case of "acquired" renal glycosuria; no development of diabetes in over four years in spite of a full diet including sugar; blood-sugar curve suggests lowered sugar tolerance.

	Blood-sugar mg. per 100 c.c.	Urine glucose.	
		Per cent.	Gm.
Fasting.....	120	Trace.	Trace.
100 gm. glucose:			
21 minutes later...	181	Trace.	Trace.
38 minutes later...	217		
64 minutes later...	200	0.90	0.23
117 minutes later..	149	0.71	1.42

of sugar in his urine with a blood-sugar of 120 mg. per 100 c.c. and higher. His blood-sugar curve was high prolonged (see Table 26). He was asked to abstain from all sugar or sugar-containing foods. He did not follow this advice, but chose to eat as his fancy dictated. Five years later, at the age of seventy-one, he is feeling well and carrying out the practice of medicine successfully; during these five years the glycosuria has persisted in traces, but there have been none of the other accepted signs of diabetes mellitus. This series of events gives us undeniable evidence that renal glycosuria may be an acquired condition and is not necessarily a congenital anomaly, and furnishes us with one more example of renal glycosuria that has persisted over a long period without developing diabetes.

Since the above article has been written a reprint from Dr. Francis H. McCrudden, assistant medical director of the New England Mutual Life Insurance Company, has been received. Dr. McCrudden, after an exhaustive and very valuable review of the literature, comes to practically the same conclusions in regard to the interpretation of sugar tolerance tests and the

significance of intermittent or constant traces of sugar in the urine as are offered in the present contribution.

CONCLUSIONS

(1) A classification of blood-sugar curves is proposed (see Table 6).

(2) Every case of diabetes mellitus exhibits a high prolonged curve; though there are very many conditions in which a high prolonged curve is not associated with diabetes mellitus.

(3) Many individuals in whom intermittent glycosuria occurs, that is not readily diagnosed as diabetes mellitus, do not suffer with this disease; among such cases an extraordinary number of instances of renal glycosuria is found.

(4) Renal glycosuria may be an acquired functional disturbance; the present series of observations bears out those who believe that renal glycosuria is a harmless anomaly and bears no relation to diabetes mellitus.

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CLINIC OF DR. WALTER A. BASTEDO

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DIGITALIS HYPERSUSCEPTIBILITY AND DIGITALIS DOSAGE

Eggleston's Contribution. Evidences of Digitalization. Cases of Hypersusceptibility. Pardee's Findings. Rate of Disappearance from Body. Persistence of Effect. Preparations. Difficulty of Standardization. Summary on Dosage and Administration. When to Stop Digitalis.

IN 1915 Cary Eggleston brought forward two revolutionary thoughts in the clinical conception of the use of digitalis, namely, (1) that the amount of digitalis necessary in any given case might be calculated in advance, and (2) that by using much larger doses than customary the desired effects might be obtained with promptness from mouth administration. He stressed the fact that whether given in small doses or large, a certain definite amount of digitalis is required for digitalization of any given heart; and he showed that while small doses such as were usually given required days to bring about such digitalization, doses by mouth large enough to digitalize in a few hours might be given with safety. These epoch-making dicta have been largely justified by the subsequent experience of clinical observers.

Eggleston's method is practically as follows: (1) The average amount of the drug itself required therapeutically to digitalize the human heart is 0.0146 times the number of pounds the patient weighs expressed in grams, or for the official tincture, which is of 10 per cent. strength, ten times this amount expressed in cubic centimeters. In the English system this is practically $2\frac{1}{4}$ minims of the tincture per pound, 240 minims for

107 pounds, 335 minims for 150 pounds, and 390 minims for 175 pounds. Thus the average effective dose of the tincture for an adult is from 4 to 7 drams.

(2) The method of administration when the patient has not received digitalis within the preceding ten days is: (a) If the case is urgent to give from one-third to one-half of the calculated amount at the first dose, one-fifth to one-fourth six hours later, and one-eighth to one-sixth after a second six-hour interval. If more is required give one-tenth of the total dose every six hours till digitalization is accomplished. (b) If the case is not urgent, as is usual, give one-fourth of the calculated total at each of the first two doses six hours apart, and thereafter one-tenth to one-eighth of the total every six hours.

(3) When the patient has been taking digitalis within the preceding ten days the doses must be kept much smaller.

The reasons for giving the calculated amount in divided doses are: (1) The lack of uniformity in preparations, and (2) the fact that though the calculated amount is approximately correct in the majority of cases, and some patients are very resistant and require enormous amounts to produce digitalization, yet others are very susceptible and show toxic symptoms with less than the calculated doses. These latter are of special interest because of the danger of digitalis poisoning. And it is both on account of a reasonable frequency of these "digitalis susceptibles" among my own patients, and because we have heard from druggists of prescriptions issued for these very large doses to be given to patients at home, a very dangerous and unjustifiable practice, that we feel it necessary to sound a warning. We would therefore repeat Eggleston's statement, that the use of his large doses is "*not a safe procedure unless the patient can be under nearly constant observation and unless the effects of treatment can be graphically recorded at frequent intervals.*"

What Are the Evidences That the Patient is Digitalized?—

It is difficult to say just what symptom or symptoms would suggest that the maximal safe dosage has been reached. It goes without saying that if the desired result is obtained the dosage is adequate and more is contraindicated. Nevertheless fre-

quently with or without the attainment of the desired result one or other symptom or group of symptoms of toxic nature may supervene and advise us that the dosage has reached the limit of safety. Clinically in our experience the earliest such symptoms or group of symptoms may be headache, "wooziness" and anorexia, nausea and vomiting, or coupled rhythm. Occasionally it is premature beats, heart-block, sinus arrhythmia or phasic arrhythmia. Graphically it may be prolonged P-R interval, flattening or inversion of the T-wave, or inversion of the P-wave.

Cases of Hypersusceptibility.—From among our many cases of hypersusceptibility we have selected a few for illustration:

Case I.—Dr. T. Approximately 150 pounds. Died of angina pectoris at age of sixty-three. For many years had occasional transient attacks of premature beats associated with nervous strains, but whenever sphygmocardiograms and electrocardiograms were taken these proved normal. In last three or four years had several transient attacks of auricular fibrillation, and one of auricular flutter in which he was seen by me. In these attacks two doses of 20 minims of tincture of digitalis invariably in about twelve hours made heart-block with pulse of about 40. Digitalis 4 grains.

Case II.—J. C. Man, 170 pounds, fifty years of age. Marked mitral stenosis and aortic insufficiency with auricular fibrillation. Thirteen tablets of digitan, one every three hours, brought heart from 140 with pulse deficit of 25 to regular rhythm with pulse 50. Digitalis $19\frac{1}{2}$ grains.

Case III.—Mrs. C. Woman about 125 pounds. Auricular fibrillation. Infusion \mathfrak{v} iv every four hours for six doses (21.6 grains at outside) produced complete heart-block.

Case IV.—L. K. Woman 120 pounds. Mitral stenosis and insufficiency. Normal rhythm. Tincture of digitalis \mathfrak{xx} , a single dose, on several different occasions in four years produced numerous premature beats.

Case V.—M. S. Woman 100 pounds. Mitral stenosis and aortic insufficiency. Normal rhythm. Tincture of digitalis \mathfrak{v} daily for one or two weeks produced serious symptoms with

many premature beats. This occurred on three different occasions in as many years.

Case VI.—P. Man, approximately 140 pounds, with cirrhosis of liver and normal rhythm. Nine tablets of digitan produced auricular fibrillation followed by complete heart-block with rate 42. Two days after the digitalis was stopped the heart-block had ceased and the auricular fibrillation effects were manifest in the ventricle with pulse about 135. Next day the heart showed normal rhythm, rate 100. Digitalis $13\frac{1}{2}$ grains.

Case VII.—V. P. Man, approximately 150 pounds, normal rhythm and lobar pneumonia, 13 tablets digitan in three days brought pulse from 110 to 62. Digitalis $19\frac{1}{2}$ grains.

Case VIII.—A. F. Woman, about 120 pounds on admission, very ill with mitral stenosis and auricular fibrillation. Cardiac rate 112 to 120 and deficit 8 to 20. Digipuratum by hypodermic 1 c.c. every four hours for six doses brought pulse to 72 without deficit and increased urine output from 26 to 64 ounces on third day. Digitalis 9 grains.

Case IX.—K. Man, approximately 140 pounds, with auricular fibrillation. Phasic arrhythmia not synchronous with the respiratory phases followed 40 minims of digalen and 6 tablets of digipuratum. Digitalis about 13 grains.

Case X.—M. L. Woman, approximately 140 pounds with auricular fibrillation. Powdered digitalis, $1\frac{1}{2}$ grains four times a day for four days, resulted in short alternating periods of coupled rhythm (ventricular beat 140, radial pulse 70) and auricular flutter (auricular beat 372, ventricular 186). Digitalis 24 grains.

We could cite many more such cases and have seen many in the literature in other connections. For example, Luten reports advanced toxic rhythms in 3 cases from 10, 19, and 19 c.c. respectively of the tincture, 1 case dying five hours after the administration of 19 c.c. The following cases reported by Christian show decided effects from what we judge to be smaller than calculated amounts though the individual weights are not mentioned:

I. In normal rhythm cases: Case V. Chronic myocarditis.

1.6 gm. (24 grains) in two days. Pulse reduced from 85 to 60. Urine increased from 625 to 2300 c.c.

Case IX. Aortic and mitral insufficiency. 1.4 gm. (21 grains) produced marked decrease in the size of the liver without change in rate or urine output.

II. In cases with auricular fibrillation: Case II. Mitral stenosis and regurgitation and aortic regurgitation. In three days 1.3 gm. (19½ grains) reduced pulse from 190 to 70, with loss of pulse deficit.

Case III. Mitral stenosis and insufficiency. Powdered digitalis 0.7 gm. (10½ grains) in thirty-six hours reduced pulse from 120 to 80.

In this connection Pardee made a study in 9 cases with normal rhythm, 8 having no cardiac disease and 1 having valvular disease. He administered doses of tincture of digitalis by mouth and found changes in the T-wave as follows:

Case 1.—126 pounds, dose 60 minims. Maximum effect at four hours.

Case 2.—123 pounds, dose 90 minims. Early effect at two hours, decided effect at four and a half hours, and maximum effect at seven hours.

Case 3.—146 pounds, dose 120 minims. Early effect at one and a half hours, decided effect at three and a quarter hours, maximum at seven hours.

Case 4.—137 pounds, dose 120 minims. Early effect at five hours, decided effect at twelve hours, maximum effect at twenty-four hours. This was the most resistant case.

Case 5.—133 pounds, dose 120 minims. Early effect at three hours, decided effect at four hours, maximum effect at six hours.

Case 6.—118 pounds, dose 130 minims. Early effect at three hours, decided effect at four hours, maximum effect at twelve hours.

Case 7.—200 pounds, dose 180 minims. Early effect at two hours, decided effect at four hours, maximum effect at five and a quarter hours.

Case 8.—90 pounds, dose 90 minims. The first electrocar-

diagram taken at three hours showed decided effect. Maximum effect at seven hours.

Case 9.—120 pounds, dose 120 minims. The first electrocardiogram at three hours showed decided effects. Maximum effect at six hours.



Fig. 93.

Fig. 94.

The first effect on the T-wave (a diminution of the height of the wave or a sinking of the level before the wave) appeared in 3 of the patients at two hours and in 7 at the end of three

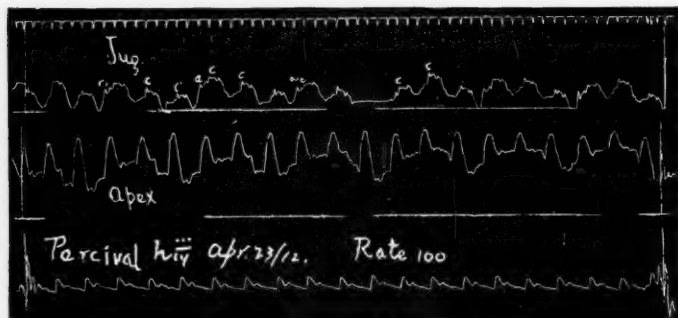


Fig. 95.—Case VI. Auricular fibrillation and complete heart-block developing in a case of cirrhosis of liver, with weak heart, but with normal rhythm. Digipuratum, $1\frac{1}{2}$ grains three times a day, was given for three days.

hours. The maximum effect on the T-wave (inversion) was present in 6 of the patients by the sixth or seventh hour and in 2 it appeared between the seventh and the twelfth hours.

Pardee also found that the average time of appearance of the first definite slowing of the rate is slightly less than for the T-wave effect, the average amount of slowing being ten beats.

Thus from mouth doses for the most part distinctly less than half the amounts calculated according to the Eggleston method, these cases with normal hearts (except one) showed very rapid digitalis effects. In fact, 1 of the patients received only $\frac{1}{2}$ minim per pound, 5 others received less than 1 minim, 2 received just 1 minim, and only 1 received more than 1 minim per pound. Pardee has observed lowering of the T-wave after a single dose

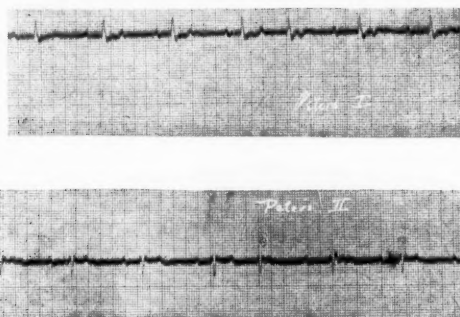


Fig. 96.—Case VII. $19\frac{1}{2}$ grains in three days produced extrasystoles, lowering of the level before the T-wave, and prolonged P-R interval.

of 30 minims of the tincture by mouth. It has been demonstrated by several observers that doses for digitalization in the adult are the same in cases with heart disease as in cases with normal hearts.

Rate of Disappearance.—Pardee further found in a series of cases that the rate of disappearance of the tincture from the body was from 10 to 40 minims a day; and he recommended that in digitalization by smaller doses extending over several days or in long-continued digitalis medication, a loss of 22 minims (average) a day be allowed for. In testing this out on clinic out-patients he found that to continue the digitalis effect after complete digitalization had been accomplished doses of

10 minims twice a day proved sufficient in most cases, while this dose three times a day frequently produced vomiting.

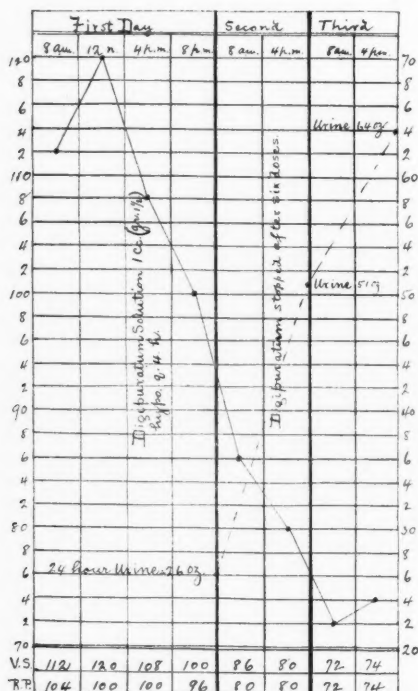


Fig. 97.—Case VIII. *Mitral stenosis and auricular fibrillation.* V.S., ventricular systole; R.P., radial pulse. Digipuratum, 6 c.c., reduced the pulse to normal rate, abolished the "pulse deficit," and increased the urinary flow, as shown above. At the same time there was a very rapid and marked disappearance of dyspnea, cyanosis, and venous engorgement. The auricle continued to fibrillate.

In our own experience as little as 5 minims a day is frequently sufficient to continue the effect, and we rarely require more than 20 minims.

Persistence of Effect.—As demonstrated by Hatcher on animals, and observed by Eggleston, Cohn, Robinson and myself in man, the digitalis action may continue as much as three

weeks or more after its administration has been stopped. I have observed persistence of partial heart-block for three and a half weeks after stoppage of the digitalis, and in several cases persistence of complete block for at least a week. Cohn showed a digitalis effect in man as late as twenty-two days after stoppage of the drug. It is therefore of very great importance to know whether or not the patient has been taking digitalis within three weeks, and if so, how much per day was being ingested and how long it has been stopped. With this knowledge our doses may be given the necessary modification, but should be continued with caution.

Preparations.—The forthcoming edition of the U. S. Pharmacopœia recognizes *powdered digitalis* assayed by the frog

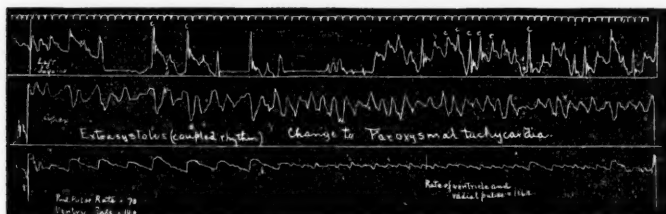


Fig. 98.—Case X.—Auricular fibrillation. Digitalis, $1\frac{1}{2}$ grains for four days, resulted in alternating periods of halving of the pulse-rate due to extrasystoles, and very rapid, almost regular pulse (auricular flutter?).

method, and two preparations, the 10 per cent. *tincture*, defatted and made by extraction with 80 per cent. alcohol, and the $1\frac{1}{2}$ per cent. *infusion* made from finely powdered digitalis and with the addition of 10 per cent. of alcohol as a preservative. The old infusion was made from the coarse leaf and was deficient in activity, but Hatcher and Weiss have shown that the new formula, using the powdered leaf, makes an infusion that corresponds in strength with the amount of leaf used in its preparation. The fluidextract, a very concentrated preparation, was so frequently found deficient in strength that it has been dropped from the Pharmacopœia. Unfortunately, when the infusion is called for many pharmacists have the habit of merely

diluting the fluidextract, and attempt to justify this action by the fact that many of the manufacturers place a formula for making the infusion from the fluidextract on their fluidextract labels. Doubtless the surest and therefore the best official preparations are the powdered leaf and the tincture.

In hypodermic use the preparations are irritating, so that intramuscular injection is preferred to the subcutaneous. For this purpose we frequently employ digitan and digifolin, which are less irritating than the tincture and are put up in ampules for the purpose.

In our present state of knowledge the use of digitalis intravenously is considered to lack the margin of safety that exists

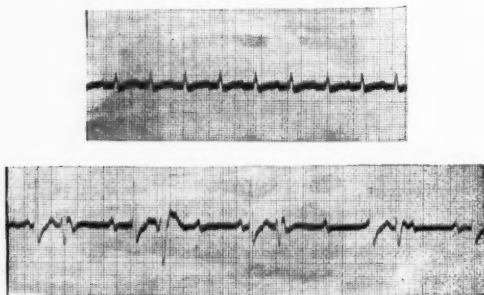


Fig. 99.—Normal rhythm. 3 drams tincture (18 grains digitalis) in five days resulted in complete heart-block and coupled rhythm.

with mouth doses. Levine and Cunningham have found intravenous digitalis just as toxic as strophanthin and ouabain and its dose less accurately determined, and Cohn and Levy have shown that comparable doses of digitalis by mouth cause undesirable effects in a much smaller percentage of cases than even the well understood strophanthin intravenously. I know of one case where the patient died while the drug was being administered, and Clarke reports two fatalities. Therefore, as we can obtain effects very quickly by hypodermic or mouth doses and digitalis by vein has not an established dose and is very dangerous, I would agree with the above investigators,

Robinson, and others in condemnation of the intravenous use of any digitalis preparation.

Difficulty in Standardization of Preparations.—Digitalis preparations are nowadays assayed, their standard of activity being based on the intravenous lethal dosage in dogs, cats, or frogs. But that this standardization is not a guarantee of uniformity in strength may be gathered from the report of the Subcommittee on Digitalis to the American Drug Manufacturers' Association at its annual meeting, June 5-8, 1922.

This committee submitted for assay to each of several experimenters three samples of the tincture of digitalis, of which

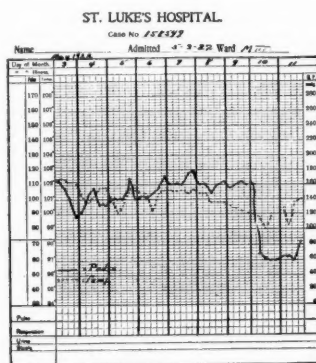


Fig. 100.—Same case as Fig. 99. Sudden reduction of pulse from 110 to 60 due to heart-block and coupled rhythm.

sample No. 1 was to be considered 100 per cent. and the others were to be compared with it. Sample No. 2 was a dilution of No. 1 made so that No. 2 had exactly 80 per cent. the strength of No. 1, and Sample No. 3 was a dilution of No. 1 made so that No. 3 had exactly 60 per cent. the strength of No. 1.

Instead of 80 per cent. the percentage strengths reported for No. 2 by the different investigators were 77.2, 67, 96.4, 89, 93, and 93.

Instead of 60 per cent. the percentage strengths reported for No. 3 were: 65.5, 57, 81.8, 64, 76, 70, and 96, this last figure

being reported by one of the strongest advocates of the cat method of assay.

These variations show the difficulties and account somewhat for the lack of uniformity in digitalis preparations. But they are not tremendous, and assayed preparations put out by reputable manufacturers may be depended upon to approximate within 20 per cent. the standard stated upon the label. Assayed preparations are therefore greatly to be preferred to the unassayed, which have been found to differ as much as 400 per cent. The factor of absorbability we cannot discuss here. The Pharmacopœia has adopted the frog method of assay.

Drops.—Do not prescribe tincture of digitalis in "drops" when you mean minims. A drop is a variable measure depending on the temperature, the fulness of the bottle, the surface from which dropped, the rapidity of dropping, etc. Even of droppers there is none official, and the purchasable droppers vary greatly in the sizes of their orifices. I have tested ordinary droppers which dropped 110, 120, 125, 137, 165, and 192 drops to the dram (60 minims). One that accompanied a bottle of tincture of digitalis which had been ordered by the physician in doses of 15 drops had such a very small orifice that it dropped 360 drops to the dram. The physician thought that he was giving 15 minims every three hours, and the child had been getting actually only $2\frac{1}{2}$ minims.

Summary on Dosage and Administration.—1. Digitalis effects may be obtained very quickly by mouth administration.

2. When full digitalis effects are desired, as in auricular fibrillation cases, the patient should be in bed and watched.

3. The drug should be stopped at the first toxic indication, for overdoses are harmful and their effects may not be readily recovered from.

4. Digitalis hypersusceptibility is encountered in a sufficient number of cases to make it of moment. We therefore recommend for the non-urgent *auricular fibrillation* or *flutter* cases either (1) A modification of Eggleston's method as follows: Having calculated the total average required dose on the basis of 0.15 c.c. or $2\frac{1}{4}$ minims of the tincture per pound of body

weight, give one-quarter of this calculated amount at once, and thereafter one-eighth every six hours till the desired effect is obtained or some evidence of digitalization becomes manifest; or (2) since busy doctors resent the need of exact figuring, give 1 dram of the tincture at once, and then $\frac{1}{2}$ dram every six hours till digitalization is evident. For digitalis powder use one-tenth of these amounts in gram or grain. For the infusion use seven times as much in cubic centimeters or minims. The same doses are applicable in fever cases, such as pneumonia. In *normal rhythm* cases much smaller doses usually suffice.

5. Till digitalization is obtained watch with the utmost care for the first signs of overdosage. In the hypersusceptible these will appear early. In the resistant the doses may be increased as soon as it is evident that effects are not being obtained.

6. Use digitalis with great caution in patients who have been taking the drug within three weeks.

7. Do not attempt to digitalize an ambulatory (office) patient. For such, however, small doses may be valuable, either of themselves or to continue a state of digitalization previously brought about.

8. To obtain good effects in normal rhythm cases it is rarely necessary fully to digitalize.

9. Intramuscular administration is called for only if the stomach is intolerant from other than digitalis causes. However, it is to be borne in mind that a sensitive stomach may very early become intolerant to digitalis, *i. e.*, before the patient is digitalized, and that a patient with such a stomach can be digitalized by the hypodermic method. Or administration by mouth may be prevented by the persistent vomiting associated with decompensation so that hypodermic doses are indicated.

10. Intravenous administration of digitalis is especially dangerous and is unnecessary. If the intravenous route is selected strophanthin should be preferred.

11. After digitalization is accomplished the effect may usually be maintained by doses of 20 or 30 minims a day, but sometimes by as little as 2, 3, or 5 minims a day.

When to Stop Digitalis.—Safety lies in stopping digitalis altogether or in materially reducing its dose when

1. *Digitalization is shown by the electrocardiograph.*

2. *The desired effect is accomplished, as by the disappearance of dropsy or enlargement of the liver, or by the slowing and steadying of the pulse in auricular fibrillation.*

3. *Nausea is marked or vomiting ensues.* An exception is mentioned in the previous section, paragraph 9.

4. *The patient complains of headache, anorexia and dizziness, or light-headedness.*

5. *The cardiac rate goes below 60.* The heart may become progressively slower for several days after the drug is stopped, hence the wisdom of ceasing the administration before the slowing has become extreme.

6. *The rate slows suddenly.*

7. *Coupled rhythm appears.*

8. *Premature beats occur.*

9. *A regular rhythm becomes irregular or intermittent.*

10. *Sinus arrhythmia* appears in normal rhythm cases or *phasic arrhythmia* in auricular fibrillation cases.

CLINIC OF DRS. MURRAY HAROLD BASS
AND HAROLD HERMAN

MT. SINAI HOSPITAL

INFECTIOUS MONONUCLEOSIS IN CHILDHOOD

CASE REPORTS

Case I.—Eleanor R., a girl aged fourteen months, who had had a pyelitis secondary to frequently repeated throat infections, was taken ill with an acute attack of what appeared to be influenza in January, 1925. The attack did not subside and the child continued to have fever ranging from 100° to 101.8° F. for three weeks. At this time the superficial lymph-nodes were enlarged, including axillary, inguinal, and cervical. The nodes were not tender and the skin over them was freely movable. Some of the nodes were the size of hazelnuts. The spleen was palpable below the costal margin. Physical examination was otherwise negative. Examination of the nasal accessory sinuses failed to reveal any evidence of infection. Urinalysis was normal. On February 18th a blood examination showed 13,400 white cells per cu.mm., with 25 per cent. polynuclear neutrophils, 7 per cent. eosinophils, 53 per cent. lymphocytes, 8 per cent. transitionals and large mononuclears, and 7 per cent. unclassified forms.

On February 24th, the low grade fever having continued, the blood was again examined, and showed only 14 per cent. polynuclears, with 1 per cent. eosinophils, 79 per cent. lymphocytes, and 6 per cent. transitionals. By March 6th the fever had subsided. The glands were receding, although they were still palpably enlarged. The spleen, however, was no longer to be felt. The blood count on this date was: Hemoglobin (Sahli) 70 per cent., white cells 18,200 per cu.mm., polynuclear neutrophils

25 per cent., eosinophils 3 per cent., small lymphocytes 63 per cent., large lymphocytes 6 per cent., transitionals 2 per cent., and myelocytes 1 per cent.

On April 7th the child was seen again. She was convalescent and the glands were almost back to normal. The white cells were only 9000 per cu.mm., but the relative lymphocytosis was still present, the polynuclears being 24 per cent., the eosinophils 2 per cent., the lymphocytes 71 per cent., and the transitionals 3 per cent. On July 22d there were no enlarged lymph-nodes and the spleen was not to be felt. The blood count was: White cells 9400 per cu.mm., polynuclears 32 per cent., lymphocytes 61 per cent., transitionals 1 per cent., large mononuclears 1 per cent., eosinophils 2 per cent., and unclassified 3 per cent.; the urine was normal. The child made an uneventful recovery.

Case II.—Stanley B., a boy aged two and a half years, was taken ill in December, 1924, with a tonsillitis which was followed by a severe aphthous stomatitis. Prior to this illness his history had been irrelevant save for frequent attacks of pharyngitis and tonsillitis. He had never had, on earlier examinations, any generalized enlargement of the lymph-nodes or spleen. During this illness it was noticed that the axillary glands were very much enlarged (walnut size), as were the cervicals. On January 14th the acute symptoms had all subsided, but the glands were still enlarged. The axillary nodes were plainly visible as they stood out anteriorly from the axillæ, but they were not tender nor was the skin reddened over them. The inguinal glands were not to be felt nor was the spleen. The tonsils were quite large and ragged, but not inflamed. Urinalysis was negative. A differential blood smear showed only 23 per cent. polynuclear neutrophils.

The boy was not seen again until March 6th, when his blood count showed 14,600 white cells per cu.mm., with only 22 per cent. polynuclear neutrophils, 3 per cent. eosinophils, 74 per cent. lymphocytes, and 1 per cent. transitionals. He looked well, but the nodes remained large in size. At this time the inguinal glands were also to be felt. The spleen could not be

palpated. His general condition and his color were good. No medicine had been given till now, when Fowler's solution, 3 drops three times daily, was prescribed.

When next seen, on April 8th, he looked very well and had gained in weight. The enlargement of the glands was still present, although it was not quite as marked as it had been. The urine remained normal. The polynuclears had increased to 40 per cent., the eosinophils were 4 per cent., the basophils 1 per cent., the lymphocytes 48 per cent., and the transitionals 7 per cent. Recovery was uneventful.

In brief, these cases show 2 young children suffering from continued low-grade fever following a sore throat, accompanied by a generalized adenopathy with enlargement of the spleen. Such cases are not at all uncommon, and since, their description by Pfeiffer has gone under the name of glandular fever. It is only within the last few years, since we have become accustomed to careful blood examinations, that it has been discovered that many of these so-called glandular fever cases may be differentiated from others by the occurrence of a relative and absolute increase in the mononuclear cells in the blood. So striking is this hematologic change that the name of infectious mononucleosis was given these cases by Cabot in 1913. Since that time a number of these cases with their peculiar blood-picture have been described in the literature, and there is a general consensus of opinion that they form a definite clinical entity.

To Pfeiffer¹ must be given the credit for reporting this condition in 1889 as a distinct clinical entity with fever, moderate enlargement of the superficial and occasionally the deep lymph-nodes, and also some enlargement of the spleen with eventual recovery. He gave to it the name of acute glandular fever. No blood counts were made on these cases. Following Pfeiffer, Park West,² in 1896, described an epidemic of this condition, but also failed to report any blood examinations. To Turk³ should be given the credit for first calling attention to certain changes in the blood which are to be seen occasionally in cases of acute infection. In 1907 he reported 3 cases of mononucleosis accompanying acute infections. Despite this suggestion, many

authors continued to report cases of acute glandular fever without studying the blood-picture. In a series of 12 cases of glandular fever which Haas⁴ reported in 1912, he failed to find anything unusual in the blood, and he stated that "the absence of blood changes characteristic of the diseases having unusual glandular enlargement for a symptom, should make the diagnosis." The following year, however, Cabot⁵ reported 4 cases with symptoms apparently those of glandular fever, but with a peculiar increase in the number of lymphocytes in the blood. He gave to the condition the name of infectious mononucleosis, and mentioned the likelihood of confusing it with acute lymphatic leukemia. In the same year, 1913, attention was again called to the lymphocytosis of acute infection by Marchand⁶ in Germany.

In 1918 Deussing⁷ reported 3 cases of diphtheria-like sore throat in boys, which was associated with a lymphoid reaction. These cases all had fever, enlargement of the lymph-nodes and spleen, and a leukocytosis of from 11,000 to 19,000 with the monocytes increased from 52 per cent. to as high as 87 per cent. These cases all recovered. In 1919 Sanders⁸ expressed the opinion that the lymphocytosis of acute infection is really an increase in the myeloid cells, the so-called lymphocytes being non-granular myeloblasts. This question has been answered by our increased knowledge of the morphology of the blood, as these cells have been found to be negative to the oxidase method of staining, thus proving them to be lymphatic in origin (Blaedorn and Houghton,⁹ Sprunt and Evans,¹⁰ Longcope,¹¹ and also our case No. 4 (R. G.).

In 1920 Sprunt and Evans, in the Johns Hopkins Hospital Bulletin, wrote an excellent report on 6 cases of infectious mononucleosis which they describe as an "acute febrile disease without local manifestations except marked lymphocytosis and slight enlargement of the glands and spleen, with recovery." These cases are interesting for their resemblance to acute leukemia. The authors observed some of their cases for as long as six years without any evidence of leukemia appearing. Pathologic examination of excised lymph-nodes in these cases during

the subacute stage showed a similarity to lymphatic leukemia, but the hyperplasia of the lymphoid cells was much less in degree. Longcope,¹¹ in an excellent paper in the American Journal of Medical Sciences in 1922, found some similarity to Hodgkin's disease in the pathologic picture of an excised gland in 2 of his cases, but this was not a striking resemblance and not at all conclusive. Blood cultures have been found negative in all cases examined. Downey and McKinlay¹² reported 9 cases of "acute lymphadenosis" which is their name for this syndrome. They gave a very excellent morphologic study of the blood, pointing out the differentiation from acute lymphatic leukemia. In lymphadenosis, unlike leukemia, there is to be found very little immaturity of the cells, which stain fairly evenly. There are great numbers of "mesolymphocytes of Pappenheim." Abortive plasma cells are found, but the changes here are largely cytoplasmic. It is more common to confuse the blood with a chronic than with an acute form of leukemia. These authors classify the lymphoid cells into three types and lay stress on the importance of differentiation of these forms in arriving at a proper diagnosis. Pathologically the picture differs from leukemia only in the degree of hyperplasia.

Infectious mononucleosis may affect people of all ages, but chiefly attacks children and young adults. Males are more often affected than females. It is an illness which usually begins with a sore throat, and therefore is frequently mistaken for so-called grippe. The nasopharyngitis which heralds its onset is not different in any way from the ordinary affection to which so many children are heir, and cultures taken from the throat have shown nothing in particular. Following the pharyngitis, the cervical and other regional lymph-nodes become enlarged. They may be moderately enlarged or may reach the size of glands seen in the course of leukemia. In most of the reported cases only the superficial nodes are mentioned. However, the deeper lying nodes may also be involved, as in the following case:

Case III.—Stanley M., a boy aged nine years, was admitted to the wards of the Mt. Sinai Hospital on July 12, 1922. This

was his second admission, his previous one having been six months prior, when he was discharged with the diagnosis of nephrosis with anasarca. At that time his blood nitrogen figures were normal, but he had a low blood-serum protein and a very high cholesterol, with marked albuminuria. His blood count was: Hemoglobin (Sahli) 88 per cent., red cells 4,960,000 per cu.mm., white cells 18,400 per cu.mm., of which 74 per cent. were neutrophilic polynuclears, 21 per cent. were lymphocytes, and 5 per cent. were monocytes.

In the interval between these admissions he had been fairly well, and had been observed in the dispensary. One month prior to the second entrance to the hospital the edema began to return. For three weeks the urine had been scant and cloudy. At the time of admission he had a cough and a swelling in the neck. There was only slight edema, but the glands of the neck were quite large, and the spleen and liver were both palpable. He was quite pale. There was some puffiness of the face and ankles. The tonsils were somewhat enlarged and ragged. The blood count on July 15th showed the following: Hemoglobin (Sahli) 88 per cent., red cells 4,500,000, white cells 20,000, polynuclear neutrophils 23 per cent., eosinophils 8 per cent., lymphocytes 60 per cent. (mostly large), monocytes 2 per cent., lymphoblasts 3 per cent., myelogones 1 per cent., myelocytes 1 per cent., myeloblasts 2 per cent. Urine contained large amounts of albumin. Blood chemistry was normal.

One week later, on July 21st, the blood-picture was: white cells 7800, polynuclears 35 per cent., eosinophils 8 per cent., basophils 1.5 per cent., myelocytes 0.5 per cent., lymphocytes 50 per cent., and monocytes 5 per cent. x-Ray examination of the chest showed enlarged hilus and peribronchial nodes. A diagnosis of "lymphemia" was made. He was discharged on August 15th very much improved.

Fifteen months later, in November, 1923, he was admitted to the hospital for the third time. He was markedly edematous, this attack having started about two weeks before with an acute upper respiratory infection. On this admission the blood count was: white cells 10,000 per cu.mm., polynuclear neutro-

phils 57 per cent., eosinophils 5 per cent., basophils 2 per cent., lymphocytes 34 per cent., and monocytes 2 per cent. There was no evidence of any glandular enlargement. Recovery had been complete, therefore, from the "lymphemia." The nephrosis was steadily getting worse, however, and during a later admission to the hospital exitus occurred and an autopsy was performed. This proved to be entirely negative insofar as the lymphatic organs were concerned.

The examination made on July 21st, after the cervical nodes had been swollen about three weeks, showed very large paratracheal and pulmonic hilus nodes such as we commonly see in Hodgkin's disease. As this boy was under observation for about three years it was possible to see the complete retrogression not only of the relative lymphocytosis but also of this glandular swelling. Moreover, this case is further instructive in that it emphasizes the harmlessness of the infectious mononucleosis, for even when this illness was engrafted upon so serious an ailment as nephrosis, the patient made an absolutely good recovery from it.

The great importance of knowing about this illness rests upon two facts—first, that on superficial examination it very closely resembles a very serious, invariably fatal malady, acute leukemia, and second, that its prognosis is almost without exception favorable. How very closely this illness can simulate leukemia is well illustrated by the following case:

Case IV.—Richard G., aged four years, had been under our observation since birth. Except for a congenital ptosis and a very marked idiosyncrasy to cow's milk leading to severe anaphylactic reactions, the past history was negative. He had had a few attacks of follicular tonsillitis and his tonsils had been left somewhat enlarged. On March 20, 1924 he was seen because he had complained of sore throat and had had slight fever. Examination showed the boy flushed with high temperature, but lively and apparently not very sick. The tonsils were much swollen and reddened, but without exudate. On the soft palate there were a number of petechial hemorrhages. The cervical

nodes were enlarged to about the size of lima beans; epitrochlear and inguinal nodes were also palpable. To our great surprise the spleen, which had never previously been palpable, was felt at the crest of the ilium. It was hard, the edge and notch being easily felt. The liver was felt two fingerbreadths below the ribs. Blood count showed the following: Hemoglobin (Sahli) 90 per cent., red cells 4,672,000 per cu.mm., white cells 10,100 per cu.mm., platelets 189,000 per cu.mm., polynuclears 11 per cent., eosinophils 1 per cent., lymphocytes 88 per cent., the Pirquet test was negative; the Wassermann test was negative; the urine was normal.

The boy continued running moderately high fever for about a week. At no time did he appear very ill. He was seen by a number of physicians, all of whom agreed that we were probably dealing with a severe form of lymphemia, an infectious mononucleosis. The boy was treated by keeping him in bed and administering a course of hypodermic injections of sodium cacodylate, beginning with 5 minims and increasing up to 15 every other day. It was planned to subject the spleen to x-ray exposures, but this procedure was found to be unnecessary, as the boy responded well to rest and arsenic. During the next few months the spleen gradually diminished in size, so that when examined on June 8th it was only just palpable. The course of the change in the blood count is shown in the following table:

	White blood-cells.	Polynuclear neutrophils, per cent.	Eosinophils, per cent.	Trans.	Lymphocytes, per cent.
March 29th.....	10,100	11	1	..	88
April 3d.....	11,500	18	1	1	80
April 7th.....	11,300	21	1	1	77
April 25th.....	14,000	28	4	5	63
July 8th.....	12,500	34	5	1	60
October 10th.....	12,500	33	6	..	61

At this time the boy's tonsils were removed and he continued to make a perfectly good recovery.

You will note here the great resemblance to leukemia, the enormous size of the spleen, the enlargement of the lymph-nodes, the huge tonsils, the hemorrhagic spots on the palate, the

great diminution in polymorphonuclear cells, only 11 per cent., with a rise in the lymphocytes to 88 per cent. Given this symptom complex, the diagnosis of acute lymphatic leukemia might easily be made. Indeed, in this very case we could not be sure that the disease was not leukemia until the child had been very carefully observed and especially the blood studied with great precision. Against the diagnosis of leukemia is first and foremost the absence of any immature or abnormal forms of white cells. Unless the lymphocytes are stained by means of the oxidase stain we cannot be certain that they are not young forms of granular cells (*i. e.*, myeloblasts or myelocytes). The absolute decision of the type of cell with which one is dealing becomes of extreme importance, and the best hematologists must be consulted in a case such as this, which so closely resembles leukemia.

The second important feature differentiating the two diseases is the reaction of the red cells. The lowest red cell count shown by our patient was 4,672,000 per cu.mm., the lowest hemoglobin was 78 per cent.; nor did he develop anemia at any stage of the illness. This absence of anemia results in the children looking quite different from those suffering from leukemia—the waxy pallor of the latter illness being conspicuously absent. It is especially interesting to note in this case that a spleen extending down as far as the crest of the ilium could, as convalescence progressed, shrink until it could no longer be palpated.

There are two other illnesses, namely, typhoid and tuberculosis, both of which may be associated with lymphocytosis and fever, which must be differentiated from infectious mononucleosis. The following case is a good example of the difficulty with which this diagnosis is sometimes made:

Case V.—Samuel L., a patient of Dr. B. S. Denzer, was two and three-quarters years old, the first of 2 children, and had a negative previous history. He was taken ill in January, 1925, with fever to 103° F., with no signs of localization anywhere. For one week the fever remained high, the next week it varied between 101° and 102° F., and then the following

two weeks it was under 100° F. in the morning and up to 101° F. in the evening. Aside from a slight cough and a recurrent urticarial eruption, there were no symptoms. A von Pirquet test and several urinalyses were normal. When the child was referred to us on February 21st his general condition was good, although he was slightly pale. There was a giant urticarial lesion on the left ear and cheek which developed while the child was being examined. A similar mild transient redness appeared on the right ear also. The heart and lungs were negative. The liver and spleen were both palpably enlarged, each being felt two fingerbreadths below the costal margin. The genitals were normal; the teeth and throat were in good condition. There was a moderate enlargement of the axillary, epitrochlear, and inguinal glands on both sides. These were not tender nor was the skin over them reddened. The hemoglobin was 76 per cent. (Sahli). The polynuclear neutrophils were only 15 per cent., with the balance mostly lymphocytes. A Widal test was negative. By March 1st the fever had not subsided, and the spleen was slightly larger. The hemoglobin was 77 per cent., red cells, 4,544,000, platelets 190,000, white cells 12,000, polynuclears 17 per cent., eosinophils 1 per cent., lymphocytes 76 per cent., and mononuclears 6 per cent.

On March 13th the hemoglobin was 80 per cent. The white cells were 11,500 and the polynuclears had increased somewhat, being 26 per cent. The eosinophils were 1 per cent., lymphocytes 67 per cent., and mononuclears 5 per cent. By this time convalescence was established, the fever having disappeared and the spleen being only just palpable under the free edge of the ribs. The glands were also beginning to get smaller.

Recovery was complete in this case.

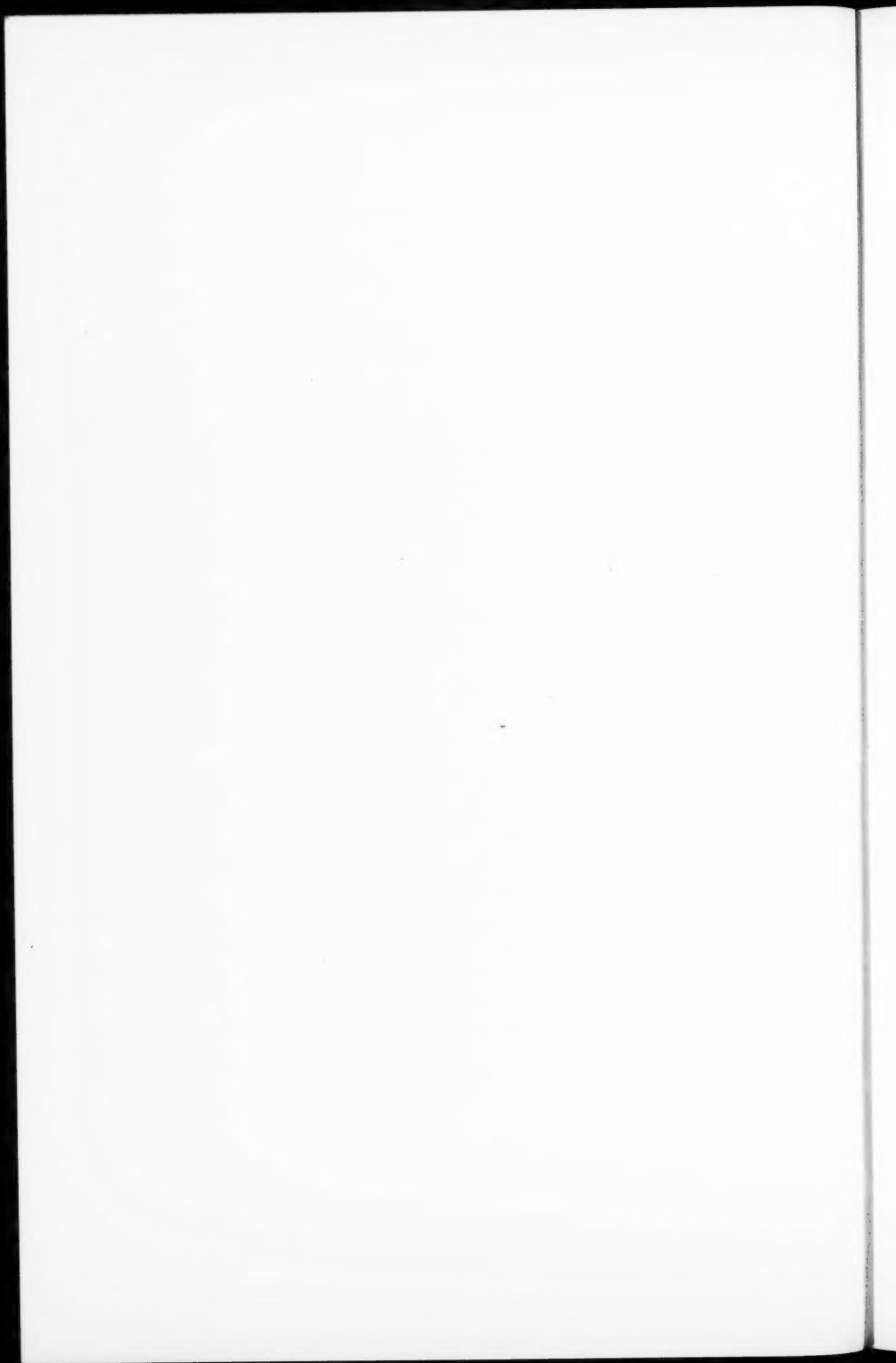
Note here the fact that this boy had been running a temperature for three weeks before a differential blood count finally cleared up the diagnosis. In this instance the superficial nodes were only moderately enlarged, so that attention was only focussed on them after the palpable spleen had been discovered.

From a consideration of the above cited typical cases we may conclude that infectious mononucleosis is a definite syn-

drome closely related to glandular fever. Its course may often be quite prolonged; it may take months before the swollen glands disappear and the blood count returns to normal. The nodes are usually not very painful and almost never go on to suppuration. The progress of the disease almost invariably leads to complete recovery.

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CLINIC OF DR. HOWARD F. SHATTUCK

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CLINICAL USE OF LIVER FUNCTION TESTS: THE ICTERUS INDEX AND ROWNTREE-ROSENTHAL SERUM DYE TEST

DURING the past few years an increasing interest has been apparent in the study of functional liver tests, in the hope that they might prove of some clinical value in the diagnosis and prognosis of diseases of the liver. Recognition of the presence of disease of this organ is possible in most instances from the routine history, physical examination, and study of the urine, feces, and blood. But even in frank cases the symptoms and physical findings give us no dependable idea of the character and extent of the functional changes that may be present. There is no definite, clear-cut picture of insufficiency in diseases of the liver, such as exists in diseases of the thyroid, kidneys, and heart. Furthermore, in the event of suspected disease of the liver, we have until recently had no tests which would enable us to detect minor hepatic disturbances or diseases in their incipency. A considerable number of liver functional tests have been devised and introduced with this end in view. Most of them have been given up as useless and unreliable, or too complicated for routine clinical use; yet they indicate the wide-spread interest in the subject.

It is known that liver function is essential to carbohydrate, protein, and fat metabolism, and to the formation of bile. The detoxicating function of the liver is not so definitely or so well established. Tests formerly described to measure these functions in hepatic disease are the levulose tolerance test, estimation of ammonia and urinary nitrogen changes, determination of the

blood lipase, and of the phenol and indol excretion in the urine. To these have been added more recently the methylene dye test and the hemoclastic test of Widal. These tests have all been given sufficient trial to demonstrate that little is to be expected from them. None is specific for the liver, nor do they show slight changes in liver function. One of the chief obstacles to finding satisfactory hepatic tests is the large margin of safety that is present in the liver. However, during the past few years, interest in dye excretion and in variations in the distribution of the biliary pigments has stimulated considerable promising work with these substances as a means of testing hepatic function.

The liver functional tests that seem to have the widest clinical application and most general use are the Rowntree-Rosenthal test for dye excretion, the quantitative estimation of bilirubinemia by means of the icterus index as described by Meulengracht, and modified by Bernheim,¹ and the qualitative and quantitative determination of bilirubinemia by the method of Van den Bergh. Because of its comparative simplicity and accuracy, we have found, as recently reported,² that the icterus index is a more satisfactory clinical method of studying liver functional changes than the qualitative method of Van den Bergh, and that it is apparently the most useful liver functional test available at present. The dye test, also, would seem to be of considerable value in estimating liver function. Sufficient work has now been done to make it clear that these two tests have a real place in the study of liver disease. This is well illustrated by the case histories which follow. Before taking up these a brief discussion of the two tests will be given.

Rowntree-Rosenthal Test.—At present the Rowntree-Rosenthal serum dye test is being widely used in the study of liver disease. This test is based on the ability of the liver to excrete the dye substance, phenoltetrachlorophthalein. Rosenthal's modification has made the test a practical and accurate one. It is based upon the rate at which the liver removes the dye

¹ Bernheim, A. R., *Jour. Amer. Med. Assoc.*, 1924, lxxxii, 291.

² Shattuck, Browne, and Preston, *Amer. Jour. Med. Sci.*, 1925 (in press).

from the blood-stream. Five mg. of phenoltetrachlorphthalein per kilogram of body weight are given intravenously; then after an interval of fifteen minutes small specimens of blood are collected, and again after one hour. The amount of dye in the serum of each specimen is determined by colorimetric comparison. Normally from 3 to 5 per cent. of the dye is present in the blood-serum at the end of fifteen minutes, and none at the end of one hour. If the liver is diseased or injured, with consequent impairment of function, the amount of dye found in the blood rises, and supposedly gives quantitative figures indicating the extent of impairment.

Icterus Index.—The liver is the sole excretory channel for bilirubin in health; we may thus consider this excretory power of the liver as an index of hepatic function. Meulengracht's method assumes that bilirubin is the only yellow pigment which normally appears in the blood-serum of a fasting person. Certain other pigmentary substances sometimes color the serum a deeper yellow after the ingestion of certain vegetables, especially carrots, which contain carotin. During fasting and under ordinary nutritional conditions, however, this factor is absent or negligible. In certain diseases of the liver or gall-bladder, and in hemolytic conditions such as pernicious anemia and hemolytic jaundice, the color of the serum deepens as a result of the increase in the bilirubin.

The test is performed as follows: Blood is collected and serum is prepared and compared in a colorimeter¹ with an arbitrary standard—a 1:10,000 potassium dichromate solution. The standard solution is put in a 15-mm. cell, and a reading taken when the standard and the serum match. The standard number, 15, is then divided by the scale reading. If the color of the serum is too deep, it is diluted and the quotient multiplied by the number of dilutions. In performing the test it is most important to avoid hemolysis of the red blood-cells, for if this takes place, even slightly, it destroys the value of the

¹ Dr. John Killian has recently prepared a disk which constitutes a permanent standard for the Klett colorimeter. This does away with the necessity of preparing a standard solution each time for the test.

test. In collecting the blood it is, therefore, most important to be sure that the needle and syringe are absolutely dry. A still better precaution is to flush them with physiologic saline solution. It is also essential that the test be performed as soon as possible after the blood-serum has been prepared.

A considerable amount of study has shown that there is jaundice of the skin and sclera when the index is above 15, and that this is not evident when the index is below 15. The normal range of the index is from 3 to 6. Accordingly, latent jaundice is represented by the figures between 6 and 16, and such figures indicate an increase of bilirubin in the blood before it is manifested by clinical jaundice. The clinical value of the icterus index in detecting latent jaundice, as well as in estimating the degree of jaundice in cases in which it has produced clinical icterus, is evident, and should be taken advantage of in studying cases of disease of the biliary tract, and of the liver.

The use of the tests is well illustrated by the following cases:

Value of the Icterus Index in Detecting Cases of Cholecystitis and Cholelithiasis Before the Development of Jaundice.—

Case I.—J. G., sixty-four years of age, was admitted to the hospital February 5, 1925, because of urinary obstruction due to hypertrophy of the prostate. He complained of difficult urination of about two months' duration, epigastric distress, and nausea. While hospitalized he had a continuous catheter. February 15th he developed an annoying cough, with little expectoration. His temperature rose to 101° F., with a slight increase in expectoration. On physical examination numerous crackling râles were heard at the base of the right lung. There was moderate epigastric tenderness. On further questioning the patient at this time, it developed that he had previously had four or five attacks of distress which he located higher up, that is, in the substernal region. These attacks had been unaccompanied by chills or jaundice. February 16th the white blood-cells were 7000; polymorphonuclears, 80 per cent. The red count was normal. The urea nitrogen in the blood was 29.4, which could be accounted for by the retention due to the

hypertrophy of the prostate. Urinalysis revealed a large amount of albumin and a few red blood-cells, but no bile. The icterus index was 15; Van den Bergh direct, negative; indirect, positive; Fouchet, positive.

Under conservative treatment the patient's symptoms disappeared four days later. Examination of the abdomen was negative, and the icterus index had fallen to 5.5, or normal. The Van den Bergh direct was negative; indirect, weakly positive; Fouchet, also weakly positive.

Comment.—The icterus index helped to confirm our impression that the attack of epigastric pain was due to gall-bladder disease, probably acute cholecystitis. This was fortified clinically two weeks later, when a similar attack was accompanied by definite jaundice. The final diagnosis was cholecystitis and cholelithiasis, with stone in the common duct.

Case II.—Mrs. E. C., thirty-four years of age, was admitted to the hospital February 20, 1925, complaining of pain in both sides of the chest, dyspnea, and pain in both lower quadrants of the abdomen which had persisted for three days. On February 5th she had been operated on at another hospital for inguinal hernia on the right side. One week later she began to cough, and the right lower quadrant became tender. The attending physician told her that she had an abscess of the abdomen, and advised her to enter Post-Graduate Hospital. On admission she had a severe knife-like pain in both sides of the chest, with "chills and fever." She was acutely ill, dyspneic, and had a flushed face. There was slight dulness and a few subcrepitant râles at the base of the right lung. The abdomen was resistant over the entire upper half, but especially on the right side. It was thought that because of the pleuritic pain and dyspnea the patient might be having a complicating right lobar pneumonia which had not yet given complete physical signs. The possibility of a localized abdominal abscess or subphrenic pathology was also considered. The leukocytes numbered 8000; polymorphonuclears, 79 per cent. The icterus index was taken because of suspected gall-bladder disease, and was

found to be 16.2. The Van den Bergh, direct and indirect, and the Fouchet test were all positive. Urinalysis was negative. An x-ray of the chest revealed slight elevation of the right diaphragm. One week after admission the patient became definitely jaundiced, and had an attack of more severe pain in the right upper quadrant, without radiation. A diagnosis of acute cholecystitis was made. The icterus index during the jaundice rose to 20.2. Ten days after the second test the index had fallen to 5.7. The Van den Bergh direct had become negative; indirect, weakly positive; Fouchet, positive.

Comment.—This patient, while suffering from complications following an operation for inguinal hernia, had severe attacks of pain in the abdomen and chest, which, in view of the fact that she had not previously been subject to indigestion, might be interpreted as due to subphrenic pathology, pneumonia, pleurisy, or gall-bladder disturbance. The first definite clue to the diagnosis was the increased icterus index of 16, which apparently indicated disturbance of the biliary tract. This was two days after the patient's admission to the hospital, and several days before she developed clinical jaundice.

Value of the Icterus Index in Determining Whether Obstructive Jaundice Has Been Relieved by Operation.—Case I. Carcinoma of Gall-bladder and Bile-ducts.—Mrs. M. C., fifty-two years of age, entered the hospital February 10, 1925. Her chief complaint was jaundice of five weeks' duration. There was no family history of carcinoma. The patient had always been well until the present illness, which began about one month before admission, with slight epigastric pain, and vomiting, but no chill. The next day she noticed that her skin was turning yellow. Since then she had become more deeply jaundiced, but had had no further pain or vomiting. The stools became putty colored and the urine coffee colored. There was moderate loss of appetite. The patient had had one previous attack of pain in the right upper quadrant in May, 1924, which lasted about twenty minutes. Following the beginning of jaundice she had a moderate dull pain in the right upper quadrant

which continued until her admission to the hospital. At that time her skin and sclerae were deeply jaundiced. The liver was not palpable, and there was no abdominal tenderness. A provisional diagnosis of cholelithiasis with stone in the common duct was made. The day after admission it was noticed that the stools were slightly brownish, and apparently contained a moderate amount of bile. During the first week in the hospital the patient continued to have deep jaundice with severe pruritis, but no other complaints. The duodenal contents contained bile and normal pancreatic ferments. x-Rays of the stomach, gall-bladder, and intestines were negative.

February 27th, as the patient's condition remained unchanged, she was operated on. Carcinoma of the gall-bladder and common and hepatic ducts, associated with cholecystitis and cholelithiasis, was found. The ducts were deep in the center of a mass of dense adhesions. A cholecystotomy with opening of the hepatic duct was made to relieve the obstructive jaundice; also cholelithotomy. The patient had a stormy convalescence and, although bile drained from the cholecystotomy opening, the jaundice did not decrease. She developed a temperature of 101° F., which rose to 103° F. on March 5th, when she died, apparently from cholemia.

The readings in the liver functional tests in this case were as follows:

- 1/ 4/25 Icterus index 143; other tests strongly positive.
- 2/13/25 Icterus index 155.
- 2/17/25 Icterus index 130; Van den Bergh, direct and indirect, and Fouchet all strongly positive.
- 2/20/25 Icterus index 144; others strongly positive.
- 2/26/25 Icterus index 150 (day before operation).
- 3/ 5/25 Icterus index 187; others strongly positive (day of death).

Comment.—Following operation, in spite of the fact that there was bile in the stools and that bile drained in considerable amounts from the cholecystotomy opening, the icterus index rose to 187. This indicated a marked obstructive jaundice, unrelieved by operation, which progressed to cholemia and death.

Value of Tests in Differentiating Between Malignancy and Severe Protracted Catarrhal Jaundice.—Case I. Catarrhal Jaundice.—Miss E. C., forty-two years of age, was admitted October 2, 1924. She had had painless jaundice for six weeks, with vomiting two or three times at the onset, and had lost 14 pounds. A diagnosis of catarrhal jaundice had been made. There was no family history of carcinoma. Soon after the onset of the present illness, the stools became "chalky" in appearance, and the urine highly colored. At the time of admission, the skin, scleræ, and mucous membranes were very deeply jaundiced. She had moderate anemia. The liver and spleen were not enlarged. x-Rays of the gall-bladder region and gastro-intestinal tract were negative. Analysis of the duodenal contents for pancreatic ferments showed reduced lipase and protease, and amylase absent. The first sample of urine showed a very large amount of bile.

The readings in the liver functional tests were as follows:

Date, 1924.	Icterus index.	Van den Bergh.		Fouchet.	Dye.	
		Direct.	Indirect.		Fifteen minutes.	One hour.
10/3	105	++++	++++	++++	15%	20%
10/6	108	++++	++++	++++	16%	20%
10/8	No clinical change in	patient's condition.				
	62 Skin and sclera still	++++	++++ icteric.	++++	16%	20%

Comment.—This case was one of severe painless jaundice of six weeks' duration, in which malignancy was suspected. The first indication that we were dealing with a benign form of jaundice was a drop in the icterus index to 62, at a time when the intensity of the jaundice was not diminished, and while the stools were still clay colored. The patient went on to a subsequent complete recovery, making the diagnosis of a benign form of jaundice clear. The Van den Bergh, Fouchet, and dye tests in this case remained elevated, so that the icterus index alone pointed in the direction of a benign form of jaundice.

Case II.—Catarrhal Jaundice.—Mrs. B. K., forty years of age, was admitted February 25, 1925, complaining of moderate epigastric distress, jaundice, and anorexia which had troubled her for one month. Her father had died of cancer of the lip, and her husband was being treated for cerebrospinal syphilis. The patient's illness had begun with a slight chill, followed by a blotchy rash over the abdomen and chest; this disappeared in two days. She then developed slight epigastric pain which passed to the right hypochondrium, and slightly to the right shoulder. The following day she became jaundiced, and as the jaundice increased the stools became colorless and the urine high colored. Her appetite was poor, and she had lost about 10 pounds. On admission the skin, scleræ, and mucous membranes were intensely jaundiced. The liver was palpable 3 cm. below the right costal margin in the mammillary line; it was smooth and not tender. The patient remained in the hospital with deep jaundice and no other symptoms except continuous loss of weight; 8 pounds in two weeks. Gastric analysis was normal; the free hydrochloric acid was 24. Analysis of duodenal contents for pancreatic ferments showed their complete absence. There was, however, a question whether this specimen was duodenal contents, but, unfortunately, the patient refused to have further specimens taken. The blood and spinal Wassermann reactions were negative. The blood-count showed moderate secondary anemia, and the urine a large amount of bile and urobilin.

February 28th the icterus index was 225; the other tests were strongly positive. The dye return was 15 per cent. after fifteen minutes, and 20 per cent. after one hour. At this time a provisional diagnosis of carcinoma of the head of the pancreas was made, and exploratory operation was undertaken. No evidence of cholecystitis, cholelithiasis, or new growth was found. Five days after operation and six weeks after onset the icterus index had dropped to 80. The Fouchet test was 2 on a basis of 4; the dye return 18 per cent. for fifteen minutes, and 16 per cent. for one hour. Twelve days after operation the icterus index was 52; dye return, 12 per cent. for fifteen minutes; 15 per cent. for one hour. Twenty-two days after operation the icterus

index was 34; dye return 5 per cent. for fifteen minutes; 0 (normal) for one hour. Two months after operation both the icterus index and the dye return were normal.

Comment.—Had operation been delayed in this case, within a few days the drop of the icterus index to 80 would have indicated that the obstructive jaundice was relieved and so was probably benign in form. Operation might thus have been avoided. The dye test in this case did not help to establish the diagnosis, but did assist the surgeon by indicating a satisfactory operative risk.

Case III.—Carcinoma of the Head of the Pancreas.—Mr. J. F., aged fifty-eight years, was admitted to the hospital November 9, 1924, because of marked jaundice. Four weeks before admission he had had severe, constant, but non-radiating pain in the epigastrium. This was accompanied by frequent vomiting and gaseous eructations. A few days later the patient noticed slight jaundice, which gradually deepened. The stools became clay colored and the urine very dark. He lost 25 pounds in four weeks. He had had flatulent dyspepsia for many years, but otherwise the gastro-intestinal history was negative. He denied syphilitic infection.

On admission he had marked jaundice of the skin and sclerae. The heart and lungs were normal, the liver was apparently not enlarged, and the spleen was not palpable. The blood-count was normal. α -Rays of the gastro-intestinal tract and gall-bladder region revealed slight enlargement of the liver. There was much bile and urobilin in the urine; the Wassermann was negative.

December 1st liver functional tests were made. The icterus index was 157; the Van den Bergh and Fouchet tests were strongly positive. The dye retained in the blood was 15 per cent. for fifteen minutes, and 20 per cent. for one hour. December 8th the icterus index was 153, and the other tests were strongly positive. The dye retention was 7 per cent. for fifteen minutes and 8 per cent. for one hour.

December 12th the icterus index was 150; the dye in the

blood was 10 per cent. at the end of fifteen minutes and 12 per cent. after one hour. The other tests were all strongly positive.

At operation, December 19th, carcinoma of the head of the pancreas was found. The liver was slightly enlarged, and there were a few small metastases on the anterior and inferior surfaces. Cholecystogastrostomy was done to relieve the obstructive jaundice.

Comment.—The icterus index remained constantly high until after the operation, which tended to show that we were dealing with a malignant and not a benign form of jaundice. One week after operation the icterus index had dropped to 60, showing that the operation had relieved the obstructive jaundice. The dye test also gave lower figures after the operation.

Value of the Tests in Cases of Cirrhosis of the Liver.—

Case I.—Mr. R. Y., aged twenty-nine years, was admitted to the hospital August 13, 1924 because of painless swelling of the abdomen of one month's duration. Six years before, while in the army, he had had dysentery for three months. The venereal history was negative. On admission there were very marked ascites and moderate loss of weight. The liver and spleen could not be palpated because of the large amount of fluid. The lungs showed signs of compression from the fluid in the abdominal cavity, and there was considerable edema of the feet and ankles.

His course in the hospital was afebrile. A provisional diagnosis of hypertrophic cirrhosis of the liver was made. Chronic pancreatitis was considered ruled out because of the marked ascites and absence of jaundice. After two weeks in the hospital the patient developed a 1 plus jaundice in the skin and sclerae. The fluid accumulation had not increased, but there was marked loss of weight. He responded early to the usual treatment for hypertrophic cirrhosis. Blood examinations showed evidence of moderate secondary anemia. The urine contained a trace of albumin, and some hyaline and granular casts, but was negative for urobilin and bile. x-Rays of the gastro-intestinal tract were negative except for a moderately enlarged spleen. The

Wassermann reaction was negative and the stools were normal. At the time of admission the phenolsulphonephthalein return was 26 per cent. in two hours.

The liver function tests were as follows:

Date.	Icterus index.	Van den Bergh.		Fouchet.	Dye.	
		Direct.	Indirect.		Fifteen minutes.	One hour.
8/13	10.7	+	++	++	12%	10%
8/18	25	++	++	++		
9/6	30	++	+++	++		
9/22	39.9	++	+++	++	10%	12%
9/30	42	++	+++	+++	12.5%	10%
10/13	45	++	+++	++	Not	done.

October 8th the jaundice and edema remained about the same, but the patient became rapidly worse, passed into coma, and died on October 13th.

Comment.—Moderate diminution of liver function was evident from the beginning, and continued. The dye test remained essentially the same throughout hospitalization. The steadily increasing icterus index was apparently the first clue to an unfavorable prognosis.

Other cases of hypertrophic cirrhosis of the liver, without jaundice, have been studied, and have shown a serum dye retention when the icterus index figures have been normal or only slightly above normal. Thus the dye test in cases without jaundice is of greater value than the icterus index.

Value of the Dye Test in Detecting the Presence of Liver Metastases Before Operation.—Case I.—B. A., a man aged fifty-two years, was admitted to the hospital in April, 1925,

complaining of epigastric distress, anorexia, nausea, and moderate loss of weight of four months' duration. Physical examination showed loss of weight and slight pallor, but no jaundice. The liver was palpable at the costal margin. No abdominal mass was felt. The stools contained occult blood. Gastric analysis revealed free hydrochloric acid, 6, and a total acidity of 14. x-Ray examination of the gastro-intestinal tract showed an infiltrating lesion involving about 4 cm. of the lesser curvature of the pyloric end of the stomach, with a six-hour retention of approximately one-tenth of the barium meal ingested.

A diagnosis of carcinoma of the stomach was made. As the patient had no vomiting, and the only indication of pyloric obstruction was a small retention of the barium meal at the end of six hours, it was decided to undertake operation, primarily with the hope of removing the new growth. The important question was whether or not metastasis to the liver had already taken place. Liver function tests were performed to determine this, if possible. The icterus index was 8.8 (zone of latent jaundice); the Van den Bergh direct reaction was negative; indirect, very mildly positive. The serum dye test showed a retention of 15 per cent. of the dye at the end of fifteen minutes, and 18 per cent. at the end of one hour. At operation an infiltrating lesion of the lesser curvature was found and, in addition, numerous metastases throughout the liver.

Comment.—In this case, although the patient was not jaundiced and preoperative examination did not show the liver to be appreciably enlarged, the dye test gave a definite indication of impaired liver function as a result of metastases implanted in its substance. The icterus index in this instance was distinctly less valuable than the dye test, and this has been our general experience in cases of liver metastases and cirrhosis without jaundice.

Value of the Tests During Arsenical Treatment for Syphilis.—

Case I.—Mrs. M. T., aged thirty-two years, came to the hospital July 3, 1924, with a diagnosis of tertiary syphilis. She had had

several operations. The venereal infection was discovered in June, 1923, when she had a chronic sore throat which led to a Wassermann being taken. This proved to be 4+. She had received three courses of salvarsan, totaling twenty-eight injections; also two courses of mercurial injections, totaling eighteen. The last mercurial treatment was given in April, 1924. In July, following further treatment with mercury, she fainted on her way home, and did not "regain consciousness until the next morning"(?) She was brought to the hospital two days later, mentally unbalanced.

Physical examination showed no jaundice, and the liver and spleen were not enlarged. The spinal fluid Wassermann was entirely negative. The blood-count was normal; the urine contained considerable acetone and diacetic acid, but no bile.

The blood Wassermann had been positive in June and October, 1923; negative in February and May, 1924; and became positive in the fall of that year.

July 5th the icterus index was 8.3; Van den Bergh indirect, slightly positive; direct, negative. The dye test was normal. Eight days later the patient became slightly jaundiced, but the liver was still not palpable. As the jaundice increased, further tests were made. The icterus index was 30; Van den Bergh indirect, slightly positive; direct, negative; Fouchet, negative. The dye test was again normal. At this time the patient went home, and was not seen again until September, when the icterus index had fallen to 14. The jaundice had disappeared and the patient felt fairly well. September 17th the icterus index was 11.2.

Comment.—As the icterus index was still in the zone of latent jaundice, it seemed unwise at this time to resume the treatment with salvarsan. It is interesting to note that the serum dye figures were always normal, and thus gave no clue to the injury to the liver from the salvarsan. In this case bismuth was substituted for the arsenical treatment until such time as the icterus index should become normal.

SUMMARY

The foregoing cases are instances of the value and limitations of the serum dye test and icterus index in the diagnosis and prognosis of liver disease. In general, it has been found that the serum dye test has its greatest value in the detection of liver disease in patients without clinical jaundice—a positive test indicating impairment of liver function; a negative one helping to rule it out. This is especially true in the diagnosis of hypertrophic cirrhosis of the liver and malignant metastases of the liver. Perhaps the greatest value of the dye test is in the study of cases with jaundice prior to operation. Here the degree of liver functional impairment can be determined with a view to deciding upon the surgical risk. It furthermore acts as a guide to the operative procedure that is to be followed in a given case. On the other hand, the test is more complicated to perform and more objectionable to the patient than the icterus index test. One observer reports several cases of ill effects from the dye test, but a large number of other workers in various parts of the country have had no such untoward experience. With further study, perhaps, other tests such as were recently suggested by Rosenthal and White¹ will make the dye test of even greater value than it now is.

There is now considerable evidence that the icterus index is the most useful liver functional test that we have for routine clinical work. It is easily and quickly performed, unobjectionable to the patient, and entirely devoid of danger. It seems to be of real value in the diagnosis of cholecystitis and cholelithiasis without clinical jaundice. It is also of great value in distinguishing between benign and malignant forms of jaundice by showing whether the jaundice is diminishing, increasing, or stationary. It also gives real aid in deciding whether the obstructive jaundice has been relieved by operation. It shows whether the liver has been injured by arsphenamin in the treatment of syphilis, and therefore acts as a guide in the further administration of the drug. There are other uses for the icterus

¹ Rosenthal, S. M., and White, E. C., *Jour. Amer. Med. Assoc.*, 1925, lxxxiv, 1112.

index not discussed here, such as the differentiation of the primary from the secondary anemias.

While the present state of development of liver functional tests marks a real advance, much remains to be done, and additional work will undoubtedly place them on a sounder basis and extend their clinical application still further.

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QUINIDIN—A USEFUL CARDIAC REMEDY

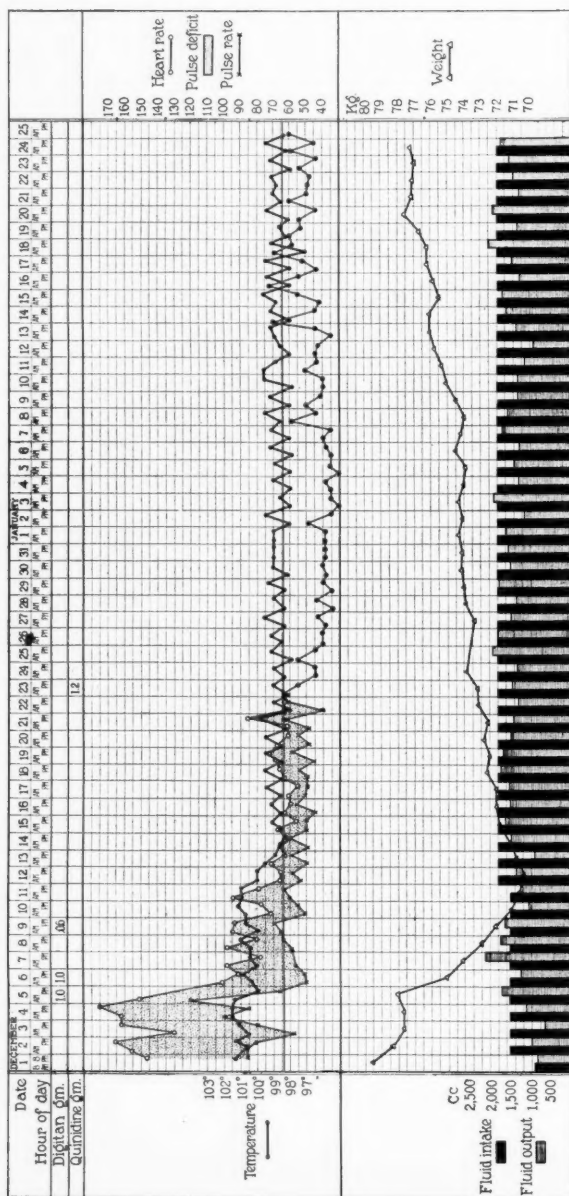
FOLLOWING the introduction into clinical therapeutics of any new drug or procedure, there are usually three phases through which medical thought apparently must pass before the value of the remedy is fairly appraised. These are: (1) A period of optimistic enthusiasm, during which glowing accounts of therapeutic triumphs are recorded and brilliant results for the future are prophesied; (2) a period of depressing nihilism, when failures are described and dangers discovered; (3) a period of rational therapeutic usage, based on a growing experience and characterized chiefly by the proper selection of cases, with due regard for both limitations and hazards.

With respect to the use of quinidin in the treatment of certain cardiac irregularities, particularly auricular fibrillation, we have gone through the first two phases of this evolutionary process. Experience with patients, critically analyzed, and experimental work on animals have increased our knowledge sufficiently so that we may adopt a point of view supported by facts.

Quinidin has been employed in the attempt to influence a variety of arrhythmias. In this clinic discussion will be limited to its use in fibrillation of the auricles. The 2 cases to be presented illustrate the successful result in: (1) Auricular fibrillation of several years' duration; (2) paroxysmal auricular fibrillation.

Case I.*—M. C. age thirty-three, single, male, was admitted to the Hospital of the Rockefeller Institute on December 1, 1921, complaining of heart trouble. He did not recall ever having

* This case is reported through the courtesy of the Hospital of the Rockefeller Institute.



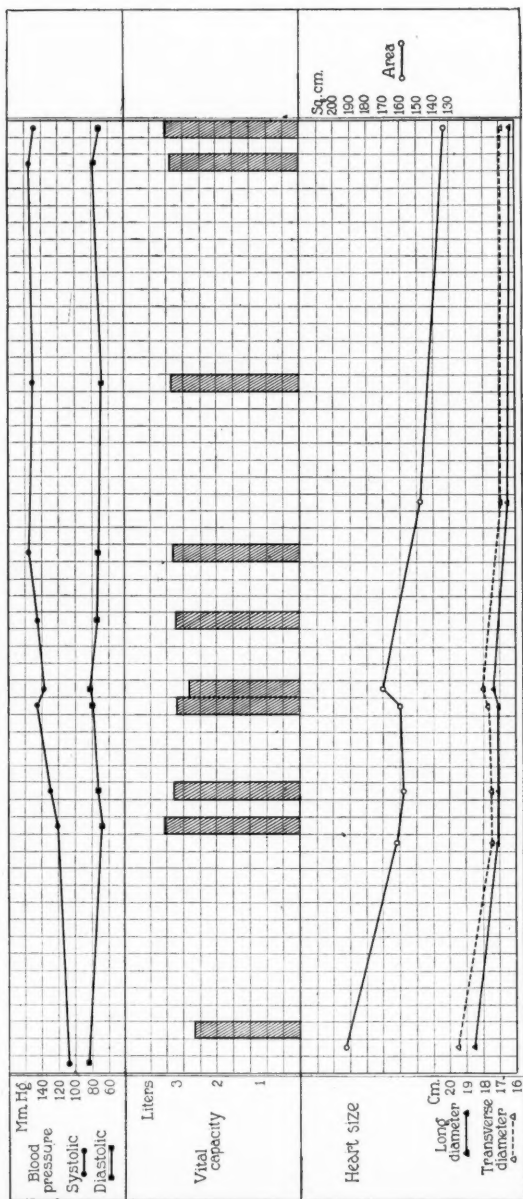


Fig. 101.—Chart summarizing the observations on Case 1.

been ill before the onset of the present illness. He worked as a shipping clerk and took practically no exercise. He smoked twenty cigarettes a day with an occasional cigar or pipe.

The present illness began about three and a half years before admission, with severe cough, which was diagnosed by his physician as due to heart trouble. He stopped work for six months, but was not confined to bed. From March 9, 1918 to March 22, 1918 he was a patient in another hospital in the city. In response to an inquiry, the following note was received from the office of the record clerk of that institution: "The pulse showed perpetual irregularity; the pulse deficit was 40." Four times during the past three years he was obliged to quit work, usually because of cough, shortness of breath, and occasional hemoptysis. He usually returned to work within two months. He stopped smoking since the onset of the present illness. He was examined for the army in the last 1918 draft and was rejected because of his heart. He stopped work two months before coming to the hospital because of shortness of breath and cough. There was no pain or edema. He took digitalis in the form of digalen irregularly, but had taken none for the two weeks prior to admission.

Physical examination showed a large, well-nourished young man. There was slight dyspnea and cyanosis. The heart was distinctly enlarged, particularly to the left, dullness extending 11.5 cm. to the left in the fifth space and 4.5 cm. to the right in the fourth space. The cardiac rhythm was entirely irregular, the rate rapid. (See Fig. 101.) There were no murmurs. There was a large pulse deficit. The blood-pressure was 108/86.

No medication was given during the first four days. On December 5th he was very uncomfortable and received 1 gm. of digitalis in the form of digitan by mouth. On December 6th he received another gram. During the next three days there was a gradual fall in heart rate with reduction in pulse deficit. There was also a sharp diuresis with a loss of 5.5 kilograms in weight. On December 9th he received another 0.6 gm. of digitalis. During the next two weeks all signs of cardiac failure disappeared.

On December 22d the patient received quinidin, 0.4 gm., at 11 A. M. and at 1 and 3 P. M. During the night the normal rhythm was restored. The patient was unaware of the altered mechanism. On January 25, 1922 (one month later) the patient was discharged from the hospital. There was some reduction in heart size. The sounds were of better quality; no murmurs were heard. The blood-pressure was 148/70. The patient was examined at frequent intervals during the next three and a half years. He returned to work and during that period passed two examinations for life insurance. He never received any more quinidin.

On June 14, 1925 the patient returned for his usual follow-up examination. He did not complain of any cardiac discomfort. It was found, however, that auricular fibrillation had recurred with ventricular rate of 150 and a large pulse deficit. During the next ten days he received 2.4 gm. of digitalis in the form of digitan. On June 24th he was readmitted to the Hospital of the Rockefeller Institute by Dr. H. J. Stewart and on June 27th received quinidin, 1.2 gm. On June 28th he received 1.6 gm. and on June 29th 2 gm. of quinidin, the doses being 0.4 gm., given at intervals of two hours. At 6 P. M. on the morning of June 30th reversion to normal rhythm was observed, the heart rate at that time being 64. For the past two months the patient has been taking quinidin, 0.2 gm., morning and evening, and thus far there has been no recurrence of the fibrillation.

Summary.—A man of thirty-three, with moderate cardiac enlargement, but no valvular disease, whose heart had probably been fibrillating for at least three years, was admitted to the hospital with heart failure. After thorough digitalization, 1.2 gm. of quinidin promptly caused reversion to sinus rhythm. The normal mechanism persisted for three and a half years without further administration of the drug, during which time the patient was able to resume his work and passed two examinations for life insurance. At the expiration of this period reversion to fibrillation was discovered in the course of a routine follow-up examination. Again after the preliminary use of digitalis, 4.8 gm. of quinidin

given during a three-day period served to restore the normal rhythm without untoward symptoms. The patient has continued to take quinidin 0.2 gm. twice daily.

COMMENT

The Choice of Cases Suitable for Quinidin Therapy.—Not every patient with persistent auricular fibrillation should receive quinidin, for two reasons. First, not every case will revert to normal mechanism, nor, if restoration is made, will this mechanism necessarily be maintained; second, by selection of cases, the danger of accident, chiefly embolism and sudden collapse, may be minimized.¹ The chief criterion of the likelihood of a successful issue is the existence of a competent myocardium. Guides in selection are as follows:

SUITABLE CASES

1. Fibrillation of recent onset.
2. Little cardiac enlargement.
3. No valvular disease.
4. Fibrillation associated with an acute infection, such as influenza or pyelitis.
5. Fibrillation associated with hyperthyroidism, provided there is only moderate myocardial damage.

In my own experience, which coincides with that of the Members of the Cardiac Club of London, as reported by Hay,² cases fulfilling the first three specifications have fared best.

UNSUITABLE CASES

1. Badly damaged hearts, especially those with marked hypertrophy and long-standing valvular disease.
2. Hearts which, after rest and proper digitalis therapy, evince but little evidence of restoration of reserve.
3. History of embolism.
4. Acute or subacute bacterial endocarditis.
5. Patients with an idiosyncrasy for cinchona derivatives.

6. Occasionally, patients giving a history of cardiac pain which has ceased after the onset of fibrillation.

If, then, these criteria are followed, it becomes clear that the number of patients suitable for the restoration experiment is distinctly limited. That is precisely the point which should be emphasized. When in doubt, it is usually wiser to counsel against the use of quinidin and to employ the more conservative method of digitalis medication. By observing this precept, the disappointment of failure is obviated and the possible hazards are slight.

Technic of Quinidin Administration.—Proper preparation before beginning quinidin is important. It is advisable to carry on the treatment with the patient in bed, under the supervision of a nurse, preferably in a hospital where electrocardiograms may be made if necessary. Heart failure, if present, must first be managed by rest, diet, regulation of fluid intake and the exhibition of digitalis. The ventricular rate should be maintained between 60 and 70 beats per minute, with the patient in bed. It is desirable to attain a maximal degree of circulatory efficiency.

The individual doses of quinidin sulphate, in capsule form, are given at intervals of two hours as follows:

First Day.—Two doses of 0.2 gm. These are given to test for the presence of idiosyncrasy to cinchona. If this be found to exist, treatment must be abandoned at once. I have seen normal rhythm ensue as a result of this small preliminary dosage.

Second Day.—Three doses of 0.4 gm.

Third Day.—Four doses of 0.4 gm.

Fourth and Succeeding Days.—Five doses of 0.4 gm.

The treatment may be continued for a week. It is safer not to give more than 2 gm. in twenty-four hours. The onset of frequent extrasystoles or of persistently high ventricular rate affords an indication for cessation of therapy. If one course is unsuccessful, a second may achieve the desired result. Usually, however, a successful issue is attained in four to six days. If it is necessary to prolong treatment beyond this period, normal rhythm, even though restored, is often not maintained. The

onset of persistent auricular flutter following quinidin is not of favorable import. Further dosage rarely converts the flutter to normal rhythm under these circumstances. It is best to stop the quinidin and administer digitalis, following which a reversion to fibrillation almost invariably ensues.

After the restoration of normal rhythm it is probably desirable to continue with the use of small, daily doses of quinidin for several weeks. The administration of 0.2 gm. morning and evening usually suffices. As is evident from the account of Case II, to be presented shortly, this amount may be taken over long periods of time without danger.

The Effects of Restoration of Sinus Rhythm.—The majority of patients with auricular fibrillation are aware of the irregularity because of palpitation. In order to maintain a relatively slow ventricular rate, constant digitalis medication is necessary. The response of the heart to effort is limited because tachycardia is readily induced. The question has been raised as to whether abolition of fibrillation is worth while. My own answer to the question is an unqualified affirmative, provided the limitations of treatment are observed and cases are carefully selected.

The permanency of normal rhythm after quinidin is variable. Selected cases have not yet been followed long enough to venture a final estimate. Certainly the result in the case just presented justified the procedure. Such a patient is better because his symptoms have been relieved; he is freed from the necessity of continuous digitalis medication; the response of the heart to effort is more effective; and he knows that his heart is beating regularly, like that of a normal person. Stewart³ has demonstrated, in a series of similar cases, a significant increase in vital capacity after resumption of normal rhythm, and has concluded, as a result of a study of the blood gases, that there is improvement in the peripheral systemic blood flow. Vital capacity determinations and measurements of heart size in our own case are shown on the accompanying chart.

Case II.—Miss W., age thirty-five, was first seen on June 22, 1923. She complained of paroxysms of irregular heart

action. One brother had rheumatic fever, with mild cardiac involvement. She had enjoyed good general health, with the exception of scarlet fever in childhood and dry pleurisy at fourteen. At fourteen, also, she had slight swelling of some of her finger-joints, lasting about ten days. At nineteen she had acute appendicitis with appendectomy. For the past ten years, she had hay-fever, and was given injections of ragweed pollen, with some relief.

The present illness began in November, 1922 (eight months previously), when she was awakened at night by pounding and fluttering of her heart. She experienced no discomfort other than the palpitation and went about her usual activities. At the end of three days the attack passed off. The paroxysm followed a nervous strain. Two weeks later (early in December, 1922) she had a similar attack, lasting this time for four days. In mid-December, 1922 (two weeks later) she had a third attack coming on after dinner, during which she had been quite upset and lost her temper. On January 4, 1923 the fourth attack occurred, appearing after breakfast and apparently unprovoked. This paroxysm lasted thirty-six hours. There was no edema, dyspnea, precordial pain, or fainting.

Examination by her physician at this time was essentially the same as when seen later by me. A basal metabolism determination yielded a value of +15 per cent. The tonsils were infected, and on January 15th tonsillectomy was performed without postoperative upset.

Fifteen days after discharge from the hospital, after walking uphill in the snow after breakfast, another short paroxysm of fibrillation occurred. During the next three months three more attacks were observed, lasting from eight hours to two days. No medication was given, the irregularity disappearing spontaneously. During this time she was leading a normal life with the exercise of moderation in her activities.

Examination on June 22d showed a rather pasty young woman, slightly overweight. The cardiac dulness was a little enlarged to the left; the rhythm was regular, the rate 100. The sounds were of good quality. There was a very faint sys-

tolic murmur at the apex and a systolic blow at the pulmonic area. Pulmonic and aortic second sounds were about equal in intensity and neither was exaggerated. The orthodiagram confirmed slight cardiac enlargement to the left. The shape of the heart was essentially normal. The electrocardiogram showed sinus rhythm with a moderate degree of left ventricular preponderance. The P-R (conduction) time was 0.15 seconds. There were no significant form changes in the curves.

It was not possible to say definitely whether organic mitral insufficiency was present. Of real import was the finding of a thoroughly competent heart muscle. The patient was advised to take quinidin sulphate 0.2 gm. after breakfast and again after the evening meal each day. She was instructed to rest after lunch and before supper for one hour. A series of bed exercises were outlined. She was told gradually to resume normal activity, avoiding, for the time being, running up and down stairs and uphill. In case of an attack of fibrillation she was told to go to bed and to take 0.2 gm. of quinidin every two hours for 4 doses.

During the summer she progressed splendidly, taking walks of 2 or 3 miles and participating in the usual social activities. She took breakfast in bed and rested for an hour after lunch. On September 16th she took a railroad journey of several hours' duration and returned to a place which, in the past, had been distinctly distasteful to her. She was apparently not fatigued by the trip. At 6 A. M. on September 17th (the following morning) she awoke with the consciousness that her heart was rapid and irregular. At 7 A. M. she took 0.2 gm. of quinidin and at 9 A. M., according to instruction over the telephone, 0.4 gm. She was seen at 12.45 P. M., at which time the cardiac rhythm was totally irregular, the rate being 138 with 130 beats felt at the wrist. The blood-pressure was 124/68. At 1.15 she was given 0.4 gm. of quinidin. At 1.40 she was aware that regular rhythm had been resumed. The rate was 112. She took no more quinidin on this day, a total of 1 gm. having been administered.

Since that day, that is, for a period of just two years, the

patient has taken 0.2 gm. of quinidin morning and evening without interruption. Her activities were gradually increased, so that at the present time she plays golf, rides horseback, dances, swims, and in short—leads a perfectly normal life. The physical signs and graphic records of the heart are essentially unchanged. The rate is generally about 80. On several occasions during the past year, the patient has been urged to omit the quinidin in order to ascertain whether normal rhythm would persist without the daily use of the drug. She has chosen, however, to continue with its use rather than to risk the possibility of a recurrence of fibrillation.

Summary.—A young woman of thirty-five with a very slightly enlarged heart and a short systolic murmur at the apex, had eight paroxysms of auricular fibrillation during a period of eight months, the majority of them associated with nervous or emotional upset. She was instructed to take quinidin sulphate 0.2 gm., morning and evening. Three months after beginning the quinidin a ninth paroxysm occurred, which was terminated in eight hours by the administration of a total of 1 gm. of quinidin. During the next two years, the patient has continued the daily use of quinidin without discomfort and with entire freedom from paroxysms. She has been able to lead a life of normal activity and, by her own preference, still continues with the use of the drug.

COMMENT

The prophylactic use of quinidin in patients subject to paroxysms of fibrillation has been brilliant. There is no danger or discomfort associated with the long-continued administration of 0.2 gm. twice or thrice daily. Usually, the 2 doses, one morning and evening, have sufficed. Many individuals suffering from this form of arrhythmia have but slight or negligible cardiac disability between attacks. Freedom from the fear of cardiac irregularity makes possible the resumption of life at a normal level. How many of these persons will, in spite of quinidin, eventually become permanent fibrillators it is not now possible to say.

THE USE OF QUINIDIN IN OTHER TYPES OF CARDIAC IRREGULARITY

Quinidin has been employed as a prophylactic in the attempt to prevent or reduce the incidence of attacks of paroxysmal tachycardia, both of auricular and ventricular origin. The results have been variable, depending in a measure on the associated cardiac condition. Further observations are desirable and may be safely undertaken.

Similarly, premature beats, when annoying to the patient, may sometimes be abolished by small doses of quinidin. Quinin will often accomplish the same end. Experience with quinidin therapy of these forms of irregularity is still meager.

SUMMARY

Quinidin is a useful cardiac remedy in the treatment of auricular fibrillation. In persistent cases when the irregularity has been present for some time, proper selection of patients suitable for therapy will insure a high percentage of successes and will guard against the possibility of untoward accident. The results of the prophylactic use of this drug in paroxysmal fibrillation have been extremely gratifying.

As a prophylactic in cases of paroxysmal tachycardia quinidin has at times been employed with benefit. Occasionally, extrasystoles may be abolished by its use in small doses. Its effects in these latter forms of arrhythmia require further study.

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BULIMIA

Disturbances of Appetite or Hunger as a Manifestation of Gastric Neurosis.—Disturbances of the sensation of appetite or of hunger, when they occur to a degree which may be considered pathologic, are properly classified among the psychoneuroses. Such disturbances may vary from complete loss of appetite and a distaste for food, on the one hand; to abnormal stimulation of appetite and hunger at the other extreme as one sees in bulimia and polyphagia; or the appetite for abnormal articles not in the category of food substances, known as pica.

Such pathologic variations occur in psychoneurotic individuals. The psychic superstructure which characterizes psychoneuroses and differentiates them from the actual neuroses is never lacking. Bulimia, akoria, pica, geophagia are not diseases, but merely represent particular symptoms of a special type of psychic neurosis characterized by appetite and hunger abnormalities. The will and act of compulsive eating may often be a conversion phenomenon in hysteria, as a compulsion hysteria; the complete loss of appetite, as seen in anorexia nervosa, may be an anxiety hysteria or an anxiety neurosis.

Hunger and Appetite.—To review a few of the facts known on the subject of hunger and appetite:

Carlson defines hunger and appetite as "the complex of sensations that in man and the higher animals urges and compels to ingestion of food." As experienced by persons, the hunger urge is a more or less uncomfortable feeling of tension or pressure and pain referred to the region of the stomach. In normal individuals the hunger must become exceptionally strong to be

markedly painful. Ordinarily the feeling is one of somewhat uncomfortable tension accompanied by a sensation of "emptiness" in the epigastric region. The hunger feeling is periodic or intermittent; it is not a continuous sensation even when the desire for food is not satisfied. The *epigastric element* in hunger is an indispensable one, but frequently there are present accessory phenomena, such as general lassitude and weakness, headache, nausea, nervous irritability, and even fainting.

A certain degree of nervous irritability is a necessary effect of hunger of even moderate intensity (Carlson). Normal persons rarely are conscious of these accessory phenomena of hunger, recognizing only the existence of the epigastric "emptiness." Individuals of a neurotic or psychoneurotic personality may experience the feelings of weakness, restlessness, and headache to so great a degree as to crowd out of consciousness the epigastric sensation of hunger. Thus, there are people who experience headaches, the latter disappearing upon partaking of food. These are "hunger headaches," and yet the patient is often absolutely unconscious of any hunger sensation.

The hunger sensation, as shown by Boldireff, Hurst, Cannon, and Washburn, and also by Carlson, is due to waves of peristaltic activity which course over the fasting stomach from three to five times a minute. These waves and tonus states are visible and can be registered on a kymographic drum. They give rise to afferent stimuli which are carried to parts of the brain and are connoted and experienced as a mildly painful sensation which is interpreted as hunger. Hunger waves usually take place in the fasting and empty stomach, but may also, in hyperirritable persons, occur before the viscus is quite emptied of its meal residue.

There has been much discussion among physiologists as to the differences between appetite and hunger. Appetite usually accompanies hunger, though a person who is not hungry may still evince appetite for a dessert or for a special delicacy. Hunger is the physical urge for food, regardless of kind; it is the cry for nourishment. Appetite cannot be separated from our memory of past experiences with food, its taste, smell, and appearance.

The "urge" in appetite may be only a special case of the general desire for pleasure. There can be no appetite for an article which has never been tasted.

Abnormally tense hunger sensations have been termed "bulimia." It is known also as "heiss hunger," and as canine or "wolf's hunger," "le faim canine." Bulimia is described in ancient Greek medical literature by Hippocrates, and is mentioned in the Talmud 200 years B. C. as a serious affection.

Case Report.—The following is an interesting illustration of a case:

The patient is a woman thirty years of age, married, and has 3 children. She has had no miscarriages. The tonsils and adenoids were removed some years ago. There are no physical ailments to be recorded in the past history. Her menstrual periods have been regular and of short duration.

Since she was a child, or to be more exact, beginning with the first menstrual periods, she has felt a continuous desire for food. This excessive craving for food has reappeared in her life at times of mental or psychic strain, and has disappeared sometimes for years, when peace of mind and mental contentment characterize that phase of her life. The illness is constituted by exalted appetite. She begins to eat at 7.00 A. M., and takes coffee, milk, or liquids. She cannot wait for solid food. She eats every hour until midday. She then has chicken soup, vegetable, dessert, tea, and plenty of bread and butter, though the amount she eats at each meal is usually not greater than that of a normal person with healthy appetite. About 2.00 P. M. she again eats, and at 4.00 and 5.00 P. M. she has another small meal. At 6.00 P. M. she has poached eggs and coffee, and she eats at 9.00 and 11.00 P. M., and at 2.00 and 5.00 A. M.

She drinks milk throughout the night. In fact, she goes to bed with 1 to 4 quarts of milk alongside the bed, and awakes at regular intervals to drink (nocturnal bulimia). She "never feels fully satisfied." Often she does not want the food, but eats to satisfy the craving and empty feeling of the epigastrium. To use her own words, "She feels as if her stomach were falling out of her." She sleeps in her corset to hold her "stomach"

tight. During the day she is weak, trembles continuously, and the desire for food overcomes her. She trembles so violently that her knees give way under her and she is obsessed with the one idea to obtain food however possible. Usually a small amount of food satisfies her. But when the desire comes over her, it must be satisfied immediately, then and there. It brooks no delay. She has been known to take a pot of hot soup off the stove, and to drink two, three, and even four soup plates full of it in rapid succession, so hot that her entire mouth and throat would be badly burned. On awakening in the morning she is torn between the double desire of immediately obtaining food and going to the toilet, and is often in an embarrassing dilemma as to which to do first.

She cries easily, is depressed over her condition, which she cannot control, but is in most other ways perfectly logical in her reasoning and well balanced in her views. She has gained within the last six months over 50 pounds, weighing now nearly 200 pounds, and requiring a new outfit of clothes almost every one or two weeks. It is impossible to send her away from home, for no hotel or boarding house would tolerate her.

Physical examination shows an overexcited woman. She is all a-tremble lest you would take so long at an examination that she will miss her next mealtime. In fact, she munches crackers at frequent intervals during the examination. The pupils are equal and normal. They react promptly. Heart and lungs are negative. Pulse is slightly fast, but regular. Blood-pressure is 135 mm. systolic and 90 mm. diastolic. Abdominal examination is completely negative. Peripheral reflexes are all markedly exaggerated.

Test-meal.—It was with great difficulty that we could obtain a test-meal, since we were never able to control her sufficiently to give her a routine Ewald or a fractional test. An extraction one hour after 4 glasses of milk showed no free and 46 total hydrochloric acid. Such an acidity is practically normal.

Radiographic examination showed a stomach which is situated vertically; the lower pole with the patient in the erect position reaches 3 inches below the crest of the ilium. The tone

was good; peristalsis normal; the duodenal bulb normal in size, regular in contour, not tender, and not fixed. With the ingestion of the barium mixture, the food at once began to pass through the pylorus of the stomach and was rapidly emptied. Observation made one and one-half hours later (the usual six-hour period could not be observed) showed about one-quarter of the food remaining in the stomach, the rest being in the small intestine. The head of the barium-zoolak column had already reached the proximal third of the transverse portion of the colon. The patient would tolerate no further observation.

This case is truly one of a psychoneurosis, the exact nature of which could not be determined. There seems to be a definite compulsion element in it; whether in the nature of a compulsion hysteria is difficult to say. It bears many of the earmarks of a hysteria. It began in youth, was initiated by the unexpected onset of the first menstruation, education of which had unfortunately been neglected by her parents. The experience recurred with every psychic strain, and was present before and after her marriage. She has been in the hands of many neurologists, psychologists, and psychoanalysts. There is no sexual irregularity to be found in her life. She is in every respect sexually normal.

Treatment.—The treatment of the case has been characterized by universal failure of every attempt to correct the condition. Psychotherapy, hypnotism, and suggestion have been tried. The patient was put to bed upon a Weir Mitchell type of rest cure. Visitors were barred; nurses were placed in attendance, and sedatives such as bromids and luminal were freely administered. The patient was constantly adjured to control her appetite, and food was supplied frequently, but in small quantities. Large doses of barbitol-sodium were supplied to assure a good night's sleep without interruption. Tincture of belladonna and tincture of xanthoxylum in doses of from 15 to 30 minims of each, three or four times a day regularly, with the idea that these drugs, being useful in the Townes-Lambert system of treating narcotic and alcoholic addicts, might also be useful in this condition to suppress the abnormal appetite.

During this course of treatment improvement was observed, a gain of weight was less rapid, the desire for food somewhat moderated, but confidence was not restored. Upon sending the patient to the country for a change of climate and atmosphere, the symptoms recurred in their original intensity. Large doses of pituitary extract by mouth and infundin by hypodermic injection failed to produce any change in the physical or mental condition. Attempts to give all solid food and to restrict fluids, hoping thereby to delay gastric emptying, were again without avail.

As far as I know, this patient, who has long since passed out of my control, is still suffering from her symptoms to an unabated degree, and, having financial means at her disposal, is still attempting to consult all the men of renown in the hope of finding one who holds the Aladdin's lamp.

The Nature of Bulimia.—The sensation of hunger is exaggerated often to an enormous intensity; the desire for food is imperious and must be satisfied often to the disregard of ethical principles in even highly ethical individuals. Bulimia is characterized by the fact that hunger comes on shortly after eating; if it is not appeased by food there follow headache, weakness, nervousness, and prostration, just as in normal hunger in most persons, only to a much greater degree. Very small quantities of food may appease this hunger temporarily. Bulimia is not the consumption of excessive quantities of food at one time (gluttony), but consists of the constantly recurring and imperious desire of food at short intervals. The demand may occur throughout the day at one- to two-hour intervals with intermissions, and may even extend throughout the night. They are often afraid to leave the house for fear that the desire for food will overtake them at an inconvenient spot, or they go walking burdened with a lunch basket. When attending theater, they will sit in the last row so that when the bulimic demand comes, they may hastily make their exit.

Appetite plays no rôle in bulimia; the hunger sensation is easily satisfied by anything in the nature of food. If no food is attainable at that moment, they may chew paper or leaves

in an attempt to appease the inordinate demand. Bulimia may occur even in the presence of anorexia. The patient may declare that she has no appetite, and is even mentally disgusted and nauseous at the sight of food, and yet must satisfy the insistent demand of hunger and the cramp-like epigastric sensation of "emptiness." It may thus occur periodically and may alternate with attacks of anorexia.

Bulimia occurs more often in women than in men. All the cases I have observed occurred in middle-aged women who were clearly and apparently psychoneurotic. A case of so-called congenital bulimia, more properly classed as akoria, is described in a girl, who from her earliest years had a voracious appetite. She could do no work, was repeatedly arrested for stealing food. During one of her paroxysms of "grand faim" she ate 32 pounds of food. Death eventually resulted from eating poisonous herbs. At autopsy the stomach was seen to be small and contracted. The condyles of the maxilla were said to have been worn away by the friction of mastication. This was undoubtedly a case of bulimia combined with akoria or pica. The accessory phenomena of hunger is also exaggerated in these persons. When the desire is upon them, the face appears pale and white, cold perspiration upon the forehead, the eyes wild looking, furtively seeking food, and the legs trembling. In order to take a clinical history it is necessary to feed them at intervals during the conversation. In 1 case x-ray examination was almost impossible, since immediately upon rising there was an imperious demand for food which had to be satisfied. At times in an attempt to satisfy hunger she would drink soup or milk in large quantities (1 to 2 liters) to the point of nausea; vomiting would ensue, but would immediately be followed by a continuance of the meal.

Constipation is the rule in bulimia, alternating, however, with attacks of persistent and severe diarrhea due to a gastroenteritis from injudicious and excessive eating.

While bulimia is essentially a symptom of a psychoneurosis or a hysteria (phobia, obsession), there is probably a gastric mechanism underlying or associated with it, one characterized by the hastened emptying of the digesting meal and the early

postprandial recurrence of exaggerated hunger contractions. It has been pointed out that in bulimia the stomach evacuation is too rapid (Ewald, Perthes, Sick, Leo, Boas). Trousseau regarded the condition as one of incontinence of the pylorus. Rosenthal quotes Bidder and Schmidt as saying that following the cutting of the vagi in dogs greatly increased hunger was noted. He considered the condition to be due to a hyperexcitability of the vagus nerves or of the vagal centers in the mid-brain. If this explanation were correct, bulimia might be considered as an autonomic imbalance phenomenon, in which because of the hastened and exaggerated emptying of the stomach an exalted hunger feeling was repeatedly aroused; the accessory phenomena characteristic of hunger, such as nervousness, headache, insomnia, and trembling, might then be considered only as a secondary neurotic manifestation of a disordered gastric emptying mechanism.

This is, however, probably inverting the real sequence of events. Our own studies have convinced us that in bulimia there is hastened gastric expulsion, food emptying so rapidly that it is practically impossible to obtain a test meal or to take radiographic plates. The gastric mechanism was otherwise quite normal. It is of interest to note that in spite of the large and frequent quantities of food ingested in bulimia, radiographic studies do not show any dilatation of the capacity of this viscus. In a case of congenital bulimia with akoria or pica described by Descuret, autopsy showed a small contracted stomach. This hastened emptying is, however, not infrequently seen in other conditions; it may be seen in some normal, though excitable, individuals; it is often seen in duodenal ulcer, in functional gastric disturbances, in carcinoma of the antrum with patulous pylorus, and in carcinoma of the fundus with reflex inhibition of the pyloric sphincter. Yet these cases do not evidence the psychoneurotic general manifestations of bulimic patients.

Because of the symptomatic similarity between bulimia and diabetes insipidus (polydipsia), it has been suggested that bulimia results from a disease or a functional disturbance of the

pituitary gland, or of the appropriate centers on the inferior surface of the forebrain or cerebrum. No structural changes were observed roentgenographically in 1 case which we studied, nor did pituitary extract by mouth or by subcutaneous injection (infundin) exert any influence upon the symptoms.

Bulimia may, however, occur as a symptom of lues, of brain tumor and of the psychoses, and some of the insanities.

Polyphagia.—It is essential to differentiate bulimia from polyphagia. The latter is a term used by many authors with various meanings and interpretations. It probably refers to the act of exaggerated and frequent partaking of food which occurs as a secondary manifestation of many of the debilitating diseases. Thus it may occur in pulmonary phthisis, carcinomatosis, in jejunal, gastric, intestinal, or biliary fistulas due to excessive loss of food from the alimentary tract before absorption has become possible, in rupture of the thoracic duct (Morgagni and Morton), and is said to occur in congenital shortening of the alimentary tract (?). It is said to occur after the operation of subtotal or total gastrectomy, though this has not been my personal experience. It occurs symptomatically in pregnancy, and is frequently seen in diabetes mellitus, Addison's disease, and in exophthalmic goiter (Basedow's disease) with rapid emaciation, and in conditions in which the basal metabolism is markedly increased.

Akoria.—By this term is meant an absence of the sensation of satiety after eating. It is a symptom of neurasthenia and of the psychoneuroses, as well as of brain tumor, cerebrospinal lues, and the psychoses and insanities. Peyer described 2 cases of akoria in outspoken cases of sexual neurosis. There is an absence of the regulatory feeling of satisfaction after eating, which while it varies within wide limits in different individuals, is normally always reached. In clinical practice I have never seen a case of akoria. Psychopathologists with large institutional experience have probably had some experience with this condition.

Parorexia.—This appellation is used to designate various types of abnormal, perverted, or depraved appetite. These con-

ditions refer exclusively to appetite rather than to hunger, at least it has not been shown that hunger is at all involved (Carlson). The abnormal appetite for highly special foods and acrid delicatessens is termed "malacia"; it is often seen in pregnancy and in adolescence of girls. Shadle mentions the case of a girl who ate 4 pounds of sugar daily to the exclusion of all other food.

Pica is the depraved appetite for articles that are not food, such as clay, chalk, and earth. There are several accounts of earth-eating (geophagia) in some of the negro races of the West Indies and Antilles. In a case of insanity reported by Davis and Stone fatal termination was caused by eating of household articles. At autopsy the cecum contained fragments of cloth, handkerchiefs, almost a whole shirt, and death had resulted from the perforation of the cecum by a large fragment of ingested wood. Instances are also recorded of the depraved appetite and the eating of slugs, beetles, cockroaches, etc. (Fulton), and of large quantities of candles and of raw beef (Johnston), as well as of domestic animals and of human excreta. The eating of such disgusting and offensive substances is known as allotriophagia and is practically confined to insane persons or extreme degenerates.

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DIAGNOSIS AND TREATMENT OF THE COMMONER TYPES OF RINGWORM

THE various reactions in the skin and its appendages caused by vegetable fungi belonging to the ringworm group are very interesting, and collectively form a group of the most frequently seen dermatoses. During the past three years about $12\frac{1}{2}$ per cent. of the admissions to the Dermatologic Department of the Vanderbilt Clinic were afflicted with some form of this disorder. The affection is especially prevalent in warm climates, where it comprises probably 35 per cent. of all dermatoses.

The clinical appearance of various lesions caused by tinea vary greatly according to location and offending fungus. Eczematized ringworm of the soles, palms, groin, and axillæ; pompholyx, disidrosis, tinea of the scalp, nails, beard, and body, and tinea versicolor are all due to a species of ringworm fungus, but the lesions are quite dissimilar. Where there are only two main families of fungi, namely, the microspora and trichophyta, there are many varieties of each.

Eczematized ringworm of the extremities is the most prevalent variety and probably the one most often unrecognized. It is a disease mainly of the summer months, although it may occur at any season of the year. It usually appears as a deep-seated, pinhead to small pea-sized grouped vesicular eruption followed by erythema and scaling (Figs. 102, 103). The eruption is often preceded or accompanied by a white, thickened, soft, soggy, and fissured condition between the toes. The favorite location for the eruption is between the fourth and fifth, and third and



Fig. 102.—Dermatophytosis or eczematized ringworm. Deep-seated vesicles over the backs and sides of the fingers, some of which have ruptured. (From the collection of Doctors Fordyce and McKee.)



Fig. 103.—Dermatophytosis or eczematized ringworm of the palm, showing numerous vesicles and bullæ and a soft, baggy, undermined skin over the palmar surface of the middle and ring fingers. (From the collection of Doctors Fordyce and McKee.)

fourth toes, beneath the arch, and along the sides of the heels. We frequently see cases of eczematized ringworm which have been diagnosed as eczema due to excessive uric acid. Many of these patients for years have been put on a diet and treated with soothing applications and warned against using soap and water. Patients often mislead the doctor by telling him that the eruption followed some digestive disorder or an acute attack of pain. I have under my care at present a woman with a marked mycotic affection of the hands, feet, and axillæ of eleven years' duration, the condition having been treated as an eczema due to a metabolic disturbance produced by renal calculi. This patient is certain that the eruption is caused or made worse by the pain.

So-called pompholyx and disidrosis, recurring bullous eruptions of the soles and palms, appearing each spring or summer, are due to a species of the ringworm fungus. Dermatitis repens, a circumscribed, soft, soggy, undermined condition of the skin of the hands and feet, is also a mycotic infection.

The eradication of these eczematized and bullous affections of the extremities often requires considerable skill and ingenuity. Usually there is no great difficulty in clearing up an attack, but there is always the probability of a recurrence, and often after observing no sign of the disease for months, the patient will have a severe attack. I know of instances where an outbreak has occurred following the wearing of shoes or gloves which had been discarded eight or ten months before. In many cases we have no explanation as to how a recurrence takes place, and it has even been suggested that the spores lie dormant in the skin for months or years, waiting for an opportunity to strike. The disease is transmitted by direct contact, and is especially prevalent among individuals who frequent public bathing places, gymnasiums, etc.

One of the most important features in the treatment of ringworm is cleanliness; daily scrubbing with soap and water followed by the free use of antiseptic remedies and germicides is imperative. The stockings should be changed each day, and the shoes at frequent intervals. After thoroughly cleansing and drying the parts, paint with liquid iocamfen, or 3 per cent.

tincture of iodine, wipe off the excess of drug with a dry piece of cotton, and dust with a bland powder. In case a more drastic remedy is necessary, apply the following:

R. Chrysarobin.....	℥ss-j
Chloroform.....	℥ij
Tincture benzoin compound.....q. s. ad.	℥j.—M.

Wipe off the excess and apply powder as above. Sometimes Whitfield's ointment,

R. Acid salicylic.....	2.0
Acid benzoic.....	4.0
Lanolin.....	30.0.—M.

is quite efficacious when rubbed on the parts night and morning. This remedy is especially indicated where a peeling effect is desired, as in dry, scaling, and thickened areas. The acute vesicular and bullous affections of the extremities are best treated by opening the vesicles and bullæ, and applying the following:

R. Bichlorid.....	gr. iij
Resorcin.....	℥ij
Acid salicylic.....	℥ij
Alcohol, 75 per cent.....q. s.	℥ij.—M.

twice daily. Where secondary infection of the bullæ with crusting has occurred, open the bullæ, cleanse with soap and water, and apply a wet dressing of 1 : 1000 to 1 : 500 of potassium permanganate. Burow's solution may be used. x-Ray is also beneficial where there is not too much secondary infection.

It was the frequent association of eczematized ringworm of the hands and feet with known tinea of the inguinal regions (Fig. 104), axillæ beneath the breasts, and the umbilical fold of the abdomen that led Sabouraud, a French dermatologist, to undertake the investigation of the former (a study) which brought about the discovery of the same type of fungus in each instance.

The affection is especially apt to occur in stout or robust individuals where there is heat, moisture, and friction of the

opposing surfaces. It is often observed in hot weather after exercise, and usually manifests itself as sharply defined, red, moist, and intensely pruritic areas. The opposing surface may become so chafed and raw as to give the appearance of having been scalded. The condition is characteristically seen between



Fig. 104.—*Tinea cruris* showing a sharply margined, slightly raised, red colored macerated scaly condition of the inguinal region, and inner and upper aspect of the thighs. (From the collection of Doctors Fordyce and McKee.)

the folds of the buttocks, and on the upper and inner aspects of the thighs where it may spread over the crotch and around the anus, giving rise to *pruritus ani*. This condition is often spoken of as "jock strap" itch or *dhobie itch*.

Scattered pinhead to much larger sized lesions may appear over the surrounding skin of the thighs and abdomen, resembling

scattered colonies on a culture plate. On rare occasions the entire skin over the body and extremities may become affected, giving rise to very distressing symptoms.

The treatment of these affected areas is much the same as that of eczematized ringworm elsewhere; that is, the free use of soap and water followed by the application of liquid iocamfen or 3 per cent. iodine, wiping off the excess and dusting on plain talcum powder. As a rule, only one to three applications are necessary at one- or two-day intervals. Between applications the free use of powder is beneficial, or in severe cases a soothing lotion such as the following is effective:

R.	Resorcin	5iss
	Zinc oxid	} āā 3ss
	Calamine		
	Glycerin	} āā q. s. ad. 3vj.—M.
	Aqua calcis		

While the use of iodine or iocamfen may seem very drastic treatment to use on the irritated surfaces, the subsequent relief justifies the temporary burning and pain. Where very large surfaces are involved, wet dressings of potassium permanganate (1 : 1000) are often very effective.

Ringworm of the scalp (Fig. 105), although occasionally seen in adults, is virtually a disease of childhood, disappearing around the age of puberty. Clinically, four different types are recognizable, the most common of which is the large, circumscribed, round or oval-shaped, partially bald areas, varying in size from that of a dime to a silver dollar, or larger. The skin over these patches is either faintly erythematous or the color of the surrounding scalp, and usually covered with fine, grayish-white adherent scales and studded with a few broken off and easily removable hairs. This type is due to the small spore ringworm fungus.

The second type is caused by the large spore fungus. The patches have the same general characteristics except that they are much smaller, varying in size from a small pea to a dime. Often they go unobserved in those with long hair.

Then there may be the numerous millet seed to pea-sized crusted and pustular lesions over the scalp due to *tinea*. This type is very hard to diagnose without cultural or microscopic demonstration of the fungus.

The fourth type (Fig. 106), or *kerion* ringworm, usually appears on the scalp or occasionally over the bearded region in men as pea to English walnut sized, bluish red colored, soft,



Fig. 105.—Multiple ringworm of scalp showing circumscribed, sharply defined oval or round-shaped partially bald, slightly scaly surface over the scalp. (From the collection of Doctors Fordyce and McKee.)

boggy swellings with sinuses discharging a thin, yellowish-red pus. The appearance of the lesion is often obscured by the yellowish colored crusts.

Due to the intimate contacts of children in play, in schools and institutions, ringworm of the scalp spreads very rapidly from one person to another, so that isolation of the affected child becomes a necessity. Because it is readily infectious, the

early recognition and riddance of the disease furnishes a problem of utmost importance to the practitioner as well as to the dermatologist.

The treatment of ringworm of the scalp has been revolutionized since the advent of the x-ray, for by its use the period of isolation has been reduced from months or even years to a short period of a few weeks.



Fig. 106.—Kerion ringworm showing a single distinct, raised, soft red area and broken-off hairs on the surface over the back of the neck. (From the collection of Doctors Fordyce and McKee.)

The technic of x-ray treatment for tinea of the scalp is quite simple and can be carried out by the skilled operator with a minimum risk to the child. The hair over the scalp is first clipped as short as possible, and the scalp washed with soap and water. A 3 per cent. ammoniated mercury ointment is then applied for three or four days in order to prevent a secondary infection. The scalp is divided into four areas (using the Kienboeck-Adamson method—Fig. 107) by beginning in the middle on a line drawn from the anterior hair line in front to the pos-

terior hair line on the back of the neck. From the center of this line measure 5 inches to just above and slightly anterior to each ear. To each of the five points (one above each ear, one in front— $1\frac{1}{2}$ inches back of the hair line—one in back, and one in the center of the head) give one unit of x-ray at right angles, using McKee factors, and shielding only the non-hairy portions.

Usually between the seventh and tenth days a faint redness appears on the scalp. At the end of the second week, when the hair begins to fall out, apply 3 per cent. tincture of iodine every

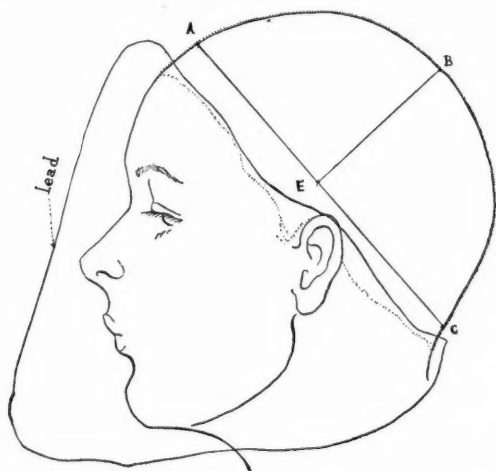


Fig. 107.

day until epilation is complete, this taking usually from three to three and a half weeks. The entire scalp then peels, leaving a shiny surface. If epilation is slow, put on an adhesive cap and pull it off, in this way removing the remaining hair. The hair begins to reappear in about two months, and in six months a full head of hair is present.

While the x-ray is a much quicker and surer method of curing tinea capitis, many cases are treated by pulling out the hairs over the affected areas and for about $\frac{1}{2}$ inch around the margins, before applying iodine or an ointment containing 25

per cent. ammoniated mercury and 4 per cent. acid salicylate. Sometimes a 10 per cent. sulphur ointment containing 5 per cent. acid salicylate is used.

Superficial ringworm of the scalp may be converted into deep type (kerion) by applying irritating remedies such as tincture of cantharides, and then treating the patient with tinea

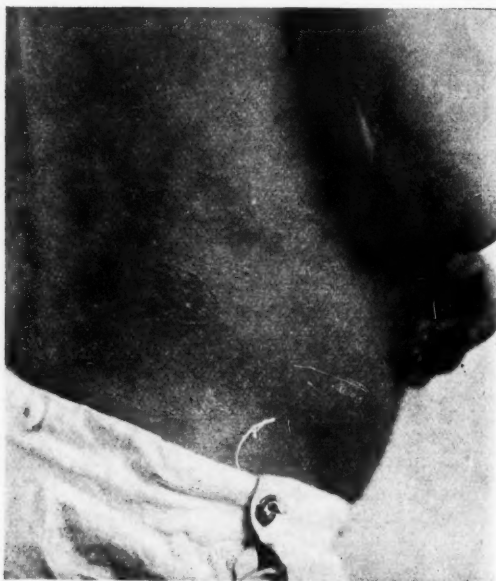


Fig. 108.—*Tinea circinata* showing a slightly scaly lesion with a clearing center and a vesicular margin of the lower right back. (From the collection of Doctors Fordyce and McKee.)

vaccine three times a week. In this way a cure can often be affected in two or three weeks. The kerion type of ringworm can be cured in the same way without using local treatment.

Tinea circinata (Fig. 108) is not infrequently secondary to tinea of the scalp and seldom offers any difficulty either in diagnosing or curing. Most often the patient makes the diagnosis himself and often cures the infection without the aid of

a physician. The lesions are characteristically oval, round, or ring shaped with clear centers, the margins being slightly erythematous, vesicular, and crusted. Either diluted tincture of iodine or sulphur ointment is sufficient to effect a cure.

Ringworm of the nails (Fig. 109) is frequently secondary to eczematized ringworm of the palms, soles, and body. Usually only a few of the nails on each hand or foot are affected. The infection most often takes place beneath the free border, the fungus first attacking the epidermis of the nail bed, causing a



Fig. 109.—Tinea of nails showing a thickened, necrotic honey-combed, scaly condition of the nails with transverse striations of the middle and ring fingers of the left hand and thumb and first three fingers of the right hand. (From the collection of Doctors Fordyce and McKee.)

dirty gray, scaly thickening which raises the nail. It gradually spreads backward toward the nail matrix, finally growing up into the nail substance itself, giving rise to an opaque, friable, necrotic, scaly condition of the nail. The skin around the base of the nail often becomes red and swollen, frequently resulting in paronychias.

In cases where the diagnosis of ringworm infection is doubtful, it is wise to collect some scrapings at the margins of the lesions, the walls of several vesicles, or a few broken-off hairs (in the case of tinea capitis), and place the material to be ex-

aminated on a glass slide to which is added a few drops of 25 per cent. sodium or potassium hydroxid. Place a glass cover over the material. Before examining, allow a period of about twenty

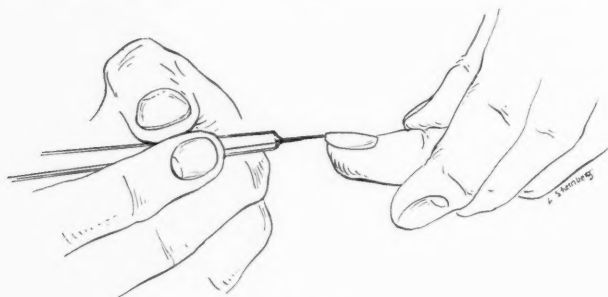


Fig. 110.

minutes to elapse, or heat the slide gently over a Bunsen burner in order to break up the scales. Examine the slide immediately with the low and high dry microscopic lens. Cultures may also



Fig. 111.

be taken; in fact, they are necessary where a differentiation of the fungus is desired.

Tinea of the nails is most effectively cured by removing the affected nails (Figs. 110, 111). If carefully done, the nails

will regrow and be perfectly normal, and there is seldom a recurrence of the tinea. Block anesthesia of the finger is often employed, or an injection of 2 per cent. novocain around and beneath the nail. Then when the skin has been separated from around the nail, the scalpel is introduced beneath the front of

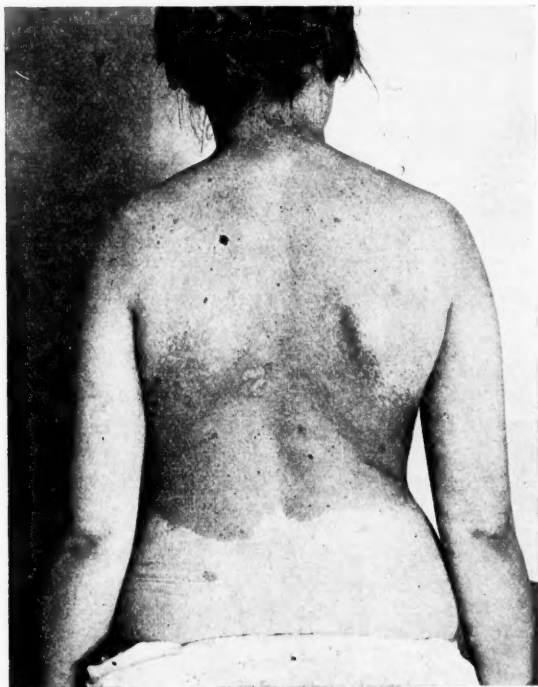


Fig. 112.—Chromophytosis or tinea versicolor showing sharply defined light brown macular and very slightly scaly band across the back and numerous small patches over the surrounding skin. (From the collection of Doctors Fordyce and McKee.)

the nail, with the point directed upward, and the nail severed from the nail bed or matrix. A hooked curet is then placed over the base of the nail and the nail gently lifted from its bed. The edges of the skin are trimmed and then painted thoroughly with 5 per cent. iodined cotton on the end of a toothpick.

The finger is dressed with borated vaselin. The painting and dressing is repeated daily for five days, after which one-half unit doses of x-ray are given at two-week intervals until three treatments have been given. The soreness usually disappears in two weeks, but it takes the nail about one hundred and thirty-five days to regrow completely.

Occasionally tinea of the nail may be cured by x-ray alone, or by softening the nail with a 35 per cent. potassium hydroxid, curetting, and applying liquid chrysarobin, iodin, or Whitfield's ointment.

While tinea versicolor (Fig. 112) is a very common affection, it seldom produces any symptoms and is either discovered during routine examination or else the patient's attention is drawn to the affection by mild itching. It is usually seen over the chest and shoulders as brownish colored, macular, very slightly scaly areas, although any part of the cutaneous surface may be affected.

The treatment is very simple and consists of daily scrubbing with soap, water and a brush, followed by application of sodium hyposulphate. It is advisable to continue this treatment for about two or three weeks after all evidence of the affection has disappeared.

SUMMARY

All eczematized and bullous conditions of the palms, soles, and interdigital spaces should be carefully investigated for ringworm fungus, as also should red, scaling, and pruritic infections in the groins, between the gluteal folds, axillæ, umbilicus, and abdominal folds.

The treatment of ringworm infections varies according to the location and type of the lesions. Generally, the free use of soap and water plus antiparasitic remedies are sufficient for relief, although x-ray is a valuable adjunct in many cases, and is especially indicated in tinea of the scalp.

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HYPERTHYROIDISM AND DOMINANT CARDIOVASCULAR SYMPTOMS WITHOUT GOITER*

Classification of Goiters.

"Forme Fruste" Types of Goiter.

Cardiovascular Symptoms of Hyperthyroidism.

Differential Diagnosis.

Treatment of Hyperthyroidism.

Three Cases of Hyperthyroidism with Cardiovascular Symptoms Without Goiter, Treated Medically.

THE recognition that overactivity of the thyroid gland is regularly associated with an increase in the basal metabolic rate has greatly simplified the diagnosis of certain types of thyroid disease. In actual practice, however, attention is not drawn to the thyroid gland as a cause of symptoms, nor is a basal metabolic test performed, unless the patient presents a more or less definite clinical syndrome of a well-recognized disturbance of the thyroid gland. This contribution is intended to present a number of patients apparently suffering from hyperthyroidism, atypical because of the absence of any thyroid enlargement, and the domination of the clinical picture by symptoms essentially referable to the cardiovascular system.

In order to adequately evaluate the clinical signs in these cases it is essential to review briefly our present conception of thyroid disease, which is still in a state of flux.

Diseases of the thyroid gland may be classified clinically or pathologically. An etiologic classification is at present precluded by the meager data upon which such a classification could be based. Development of endemic goiter as the result of iodine

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deficiency, as determined by Marine and Kimball, and the prompt drop in the basal metabolic rate, with improvement of the symptoms in exophthalmic goiter, as the result of iodine therapy in the form of Lugol's solution, first shown by Plummer, are points which may form a nucleus for a future etiologic classification. The best classification for clinical purposes is one dependent on the degree of functional activity of the thyroid as measured by the determination of the basal metabolic rate. Accordingly, we may classify goiters as follows:

A. Goiter with evidence of *excessive* functional activity of the thyroid.

1. Goiter with hyperthyroidism.
2. Exophthalmic goiter.

This should be considered as a specific syndrome of unknown etiology, but in which the overactivity of the thyroid is one of the most important factors.

3. Toxic adenoma.

B. Goiter without any changes in the functional activity of the thyroid.

C. Goiter with evidence of *diminished* functional activity of the thyroid.

In this group should be considered myxedema and sporadic cretinism, which are associated with small or rudimentary thyroids.

In all the various groups of this classification, with the possible exception of exophthalmic goiter, which is usually associated with one form of enlargement of the thyroid, we may also group cases according to the type of the goiter itself, whether it is parenchymatous, adenomatous, cystic, etc. We may also classify many of the groups according to the age incidence, such as adolescent goiter, menopause goiter, etc.

We may also recognize in all forms of goiter certain types which have been called "forme fruste" types. In these forms the symptoms are so slight that the nature of the disease may be entirely overlooked. In the types of goiter unassociated with a change in the basal metabolic rate, the only symptoms are those of mechanical pressure, or the cosmetic appearance of the

goiter itself. The "forme fruste" types in these goiters are characterized by a mass so small that it is difficult to palpate, or one which may be hidden under the sternum, and be recognized only by an x-ray picture.

A "forme fruste" type of goiter, associated with a change in the metabolic rate, may be readily recognized by the determination of the basal metabolic rate; as hyperthyroidism, when the rate is increased, and as hypothyroidism, when it is lowered. Until the general use of basal metabolic rate determinations, numerous cases of "forme fruste" types of hyperthyroidism or exophthalmic goiter were described. Many of these cases, however, despite more or less classical clinical manifestations, showed no change in the basal metabolic rate. These patients cannot therefore be considered as hyperthyroidism at all, but they have now been classified as a group of constitutional cases characterized by autonomic instability. This condition has been described long ago by some of the older writers, and in later years it has been much elaborated by Solis Cohen, Eppinger and Hess, and others, under various names. The chief symptoms of these patients are those of imperfect function of the thoracico lumbar division of the autonomic nervous system. The symptoms are extremely labile and consist of vasomotor instability, functional gastric symptoms, functional cardiac symptoms, sleeplessness, etc. They suffer a great deal from anxiety and fears. The condition is evidently congenital and hereditary. They are the patients who suffer from anxiety neuroses, constitutional inferiority, gastric neuroses, etc. They are usually thin, lanky individuals with visceroptosis, and show very little tendency to gain in weight. Their predisposition to the development of a frank exophthalmic goiter or hyperthyroidism as the result of some psychosexual shock has been recognized by many clinicians. The exact relation of this condition to exophthalmic goiter and hyperthyroidism is at present a moot question, the solution of which must await the determination of the cause of exophthalmic goiter and hyperthyroidism.

When judged by the basal metabolic rate, the number of cases of "forme fruste" types of hyperthyroidism become ex-

ceedingly rare, and they are nearly always associated with some enlargement of the thyroid gland. When such cases occur without a thyroid enlargement they are of sufficient rarity and interest to warrant discussion. Hyperthyroidism is characterized essentially by the following symptoms:

1. An increase in the basal metabolic rate beyond the upper limits for normal.
2. A loss in weight.
3. Tachycardia, palpitation, vasomotor symptoms, and other cardiovascular symptoms.
4. Enlargement of the thyroid gland.
5. Tremors.
6. Psychical symptoms such as anxiety and fears.
7. Evidence of autonomic instability, such as flushing of the skin, excessive perspiration, visceral spasms in the stomach, intestines, and other abdominal viscera.
8. Asthenia.

These symptoms may be present in varying intensity, and some of them may be so marked as to dominate the clinical picture entirely. In a previous communication¹ I presented a group of cases of definite hyperthyroidism associated with gastric symptoms. These symptoms so dominated the clinical picture that the causative hyperthyroidism was entirely overlooked until a basal metabolic determination was made.

The cases included in the present contribution were unrecognized cases of hyperthyroidism without goiter, in which the cardiovascular symptoms masked the entire clinical picture. The presence, however, of a loss in weight, tachycardia, and hypertension, suggested hyperthyroidism, which was revealed by the increased basal metabolic rate.

Cardiovascular Symptoms of Hyperthyroidism.—Boothby,² Kraus,³ and others have described cases suffering essentially from chronic cardiac failure, which on careful examination showed a slight enlargement of the thyroid gland, and which for a long time had a persistent increase in the basal metabolic rate. Recently Lahey and Hamilton⁴ described a group of cases which they termed "thyrocardiacs." These patients suffer essentially

from paroxysmal attacks of failing compensation and chronic cardiac disease in which they established a thyroid etiology by means of repeated careful basal metabolic determinations.

Cardiac symptoms in goiter with hyperthyroidism, in exophthalmic goiter and toxic adenoma, are more common than is generally described. The percentages in the literature for the incidence of such cardiac symptoms, other than the usual tachycardia, vary from 10 to 50 per cent. This apparent variation in the incidence is probably due to the fact that age is an important factor. In older patients cardiovascular changes are usually more prevalent and, in spite of definite evidence of thyroid disease, the cardiovascular changes in the older patients may be due to causes other than the thyroid, although such causes cannot always be determined at the time of examination. Perhaps a safe figure is about from 20 to 25 per cent. The cardiovascular symptoms complained of may be subjective or objective. The subjective symptoms are palpitation, periodic attacks of precordial pain or precordial distress, attacks of dyspnea, and anginal attacks.

Palpitation is one of the usual symptoms of hyperthyroidism. It may occur periodically or be persistent. Its incidence is usually in proportion to the severity of the disease. Precordial pain is a frequent symptom and is usually due to the vigorous heart action against the chest wall. Both palpitation and precordial pain are very common symptoms and may be present without any definite evidence of cardiac involvement. Attacks of dyspnea not infrequently occur in hyperthyroidism and in exophthalmic goiter. The dyspnea occurs especially at night. Many patients complain of a sense of pressure in the chest, associated with attacks of dyspnea. Anginal attacks have been described by some of the older writers and is not an infrequent symptom. It is probably due to vascular spasm of the coronary arteries.

The most common objective findings are tachycardia, vasomotor disturbances, murmurs, arrhythmias, paroxysmal attacks of auricular fibrillation, heart block, and hypertension. The

essential feature of all the cardiac symptoms in hyperthyroidism is their paroxysmal character.

Tachycardia is the symptom essential for the diagnosis of hyperthyroidism, exophthalmic goiter, or toxic adenoma. The pulse rate may vary from 100 to 160 or more. It is always present in these conditions, even when there are no other signs of cardiac involvement. Indeed, the high pulse rate and pulse pressure are almost as definite signs of hyperthyroidism as the increase in the basal metabolic rate. In general, when a goiter is associated with a rapid pulse and high pulse pressure, it is almost invariably accompanied by an increased basal metabolic rate. When, however, a goiter is not accompanied by a rise in pulse rate and pulse pressure, the basal metabolic rate is usually not increased. The most remarkable thing about the tachycardia of hyperthyroidism is the fact that, although it may be present for a long time and the rate may be very high, the patient may complain of little or no symptoms of cardiac derangement. Persistent tachycardia as a residual symptom when the hyperthyroidism has improved and the basal metabolic rate has been lowered may indicate cardiac involvement.

Vasomotor Disturbances.—Many patients with hyperthyroidism complain of symptoms which are directly or indirectly due to the labile arterioles and capillaries. These usually consist of marked flushing of the skin, especially around the chest, neck, and sometimes on the face. When the vasomotor symptoms are marked the signs may simulate aortic regurgitation. There may be a Corrigan pulse, pistol shot sound in the femorals and brachials, a high systolic pressure with tachycardia, and a very high pulse pressure. It is rarely associated with a diastolic murmur. The vasomotor symptoms may produce other symptoms such as tinnitus, dizziness, throbbing sensations, etc.

Murmurs.—Systolic murmurs heard over the entire precordium are very common in hyperthyroidism. They are blowing in character, and are usually not transmitted. In long-standing hyperthyroidism they may remain permanent, probably as an indication of permanent cardiac involvement. Presystolic roughening of the first sound, with a marked thrill, is not at all

uncommon. It does not indicate a real lesion, but is produced by the vigorous, rapid heart action. Presystolic murmurs are extremely uncommon and their occurrence is very doubtful. Diastolic murmurs are also very uncommon, although all the other signs of aortic regurgitation, such as the Corrigan pulse, pistol shot sound, etc., may be present.

Arrhythmias.—Cardiac arrhythmia is one of the well-recognized cardiac signs in hyperthyroidism. The arrhythmias are usually temporary in character and are associated with tachycardia. They frequently disappear under treatment. Krumbhaar,⁵ Dameshek,⁶ Kerr and Hensel⁷ found arrhythmias in from 2 to 20 per cent. of their cases. Krumbhaar,⁵ Dameshek⁶ and others have studied the arrhythmias in hyperthyroidism with the electrocardiograph and have recognized a paroxysmal auricular flutter, paroxysmal auricular fibrillation, and paroxysmal auricular tachycardia, and persistent auricular fibrillation. Krumbhaar,⁵ Kerr and Hensel,⁷ Stein,⁸ and others, have noticed a high T wave in the electrocardiographic tracings. They consider this singular finding as diagnostic for hyperthyroidism, and when it is flattened in Leads I and II, they think it indicates a bad prognosis. Dameshek⁶ could not find the high T wave so regularly in his cases, but he found left ventricular hypertrophy and left ventricular preponderance. Partial and complete heart block has recently been described by Dameshek,⁶ Krumbhaar,⁵ Goodall,⁹ and others. Auricular fibrillation is fairly common in hyperthyroidism and is frequently a residual symptom in improved cases.

Decompensation.—Cardiac decompensation in the course of exophthalmic goiter or hyperthyroidism is not so common, but many of such cases with dominant cardiac symptoms, in the course of the disease, are frequently left with a persistent auricular fibrillation and may develop into chronic cardiacs with prolonged attacks of decompensation, even with edema. Many such cases respond to treatment when the thyroid etiology is recognized.

Hypertension.—There has been considerable difference of opinion for a long time as to the blood-pressure in hyperthy-

roidism and in exophthalmic goiter. The study of a large series of cases, however, by Plummer,¹⁰ and others, indicates that hyperthyroidism is generally associated with a systolic increase in blood-pressure and a high pulse pressure. Dameshek⁹ has pointed out that when the cardiac symptoms are present the systolic blood-pressure is apt to be proportionately higher than otherwise. Boas and Shapiro¹¹ have recently reported a number of cases of hypertension associated with a diastolic rise in pressure, accompanied with an increased basal metabolic rate.

The significance of the increase in the basal metabolism in these cases is still in doubt. Further study of similar cases may determine whether this is evidence of hyperthyroidism or not.

SIGNIFICANCE OF THE BASAL METABOLISM

The pathognomonic sign of hyperthyroidism is the increase in the basal metabolic rate. When this is not accompanied by an enlargement of the thyroid, the etiology of the syndrome will depend on the causes which increase the basal metabolic rate. Although an increased functional activity of the thyroid is the usual cause for such an increase, other factors have been demonstrated. Aub, Boothby, and others have demonstrated that injections of adrenalin will raise the basal metabolic rate. Marine showed an increase in the basal metabolic rate after freezing or removal of the adrenal cortex. These facts seem to indicate that the adrenals also play an important rôle in maintaining the basal metabolic rate. Emotional factors have recently been shown by Ziegler and Levine¹² to be responsible for an increase in the basal metabolic rate. The question therefore arises in the cases which I am presenting, as well as in all cases of hyperthyroidism, especially without goiter, whether we are dealing with a hyperthyroidism, with a disturbance of the adrenals, or with some sustained emotional stress, any of which might, in view of the experimental work, increase the basal metabolic rate. A similar question applies to exophthalmic goiter, which is of unknown etiology and unknown pathogenesis, in view of the well-known fact that psychical shocks may instigate the syndrome.

The basal metabolism determinations in hyperthyroidism with cardiac symptoms is only valuable in those cases without dyspnea. Peabody, Wentworth, and Barker¹³ have shown that dyspnea tends to increase the basal metabolic rate and that this increase is seldom more than 20 per cent. We can therefore assume the presence of hyperthyroidism only when the rate is more than 20 per cent. above the upper limits for normal, or when dyspnea is absent.

The probability of hyperthyroidism being the cause of the syndrome in the following cases is emphasized by the fact that two of the cases responded so definitely to iodine in the form of Lugol's solution, much in the same manner as exophthalmic goiter does.

DIFFERENTIAL DIAGNOSIS

The diagnosis of hyperthyroidism, with or without goiter, is not difficult if routine basal metabolic determinations are made whenever the patient presents the triad of tachycardia, with or without arrhythmia, loss in weight, hypertension, with or without the other classical signs.

Lahey and Hamilton,⁴ in a study of thirty-eight "thyrocardiacs," most of whom were bedridden cases of chronic cardiac disease, with decompensation, have outlined the following diagnostic factors for the recognition of the thyroid etiology of such cases:

"1. Every chronic cardiac should be suspected of hyperthyroidism when no other etiologic factor is possible.

"2. Prominent or staring eyes in every cardiac should be assumed to indicate hyperthyroidism.

"3. Transient attacks of established auricular fibrillation, especially when pigmentation of the skin is present, every case with auricular fibrillation, with or without decompensation, and in which there is a discrepancy between the patient's condition, the history, and the heart findings, should be suspected of hyperthyroidism."

The cases may be distinguished from mitral stenosis, aortic regurgitation, effort syndrome, autonomic instability, etc., by

the presence of thyroid enlargement, and by the increase in the basal metabolic rate.

The following cases were being treated for various conditions for months. The first was diagnosed as hypertension, with primary cardiovascular disease, and because of the loss in weight malignancy was also suspected. The second case was treated by an otologist for tinnitus, which was the chief symptom. The third was diagnosed as acute endocarditis, because of the marked tachycardia with arrhythmia, although the usual causative factors for endocarditis were absent.

In all three cases the triad of tachycardia, with arrhythmia, hypertension, and loss in weight were present, and a basal metabolism determination readily established the diagnosis.

TREATMENT

Lahey and Hamilton⁴ have reported twenty-seven excellent results in their group of thirty-eight cases with marked improvement of the cardiac symptoms after ligation of the superior thyroid arteries. Levine and Sturgis,¹⁴ and Dameshek, have noticed improvement in the cardiac symptoms of hyperthyroidism after x-ray treatment and ligation.

The following cases are presented to demonstrate the improvement that can be obtained by the judicious use of iodine in the form of Lugol's solution. Whether this improvement is permanent or not cannot be determined until further observation. Surgical therapy was not attempted because of the absence of any demonstrable thyroid pathology, and the good results obtained by medical treatment. If a definite thyroid pathology is present, however, surgical therapy might be tried after preliminary treatment with iodine.

A CASE OF HYPERTHYROIDISM MASKED AS CARDIOVASCULAR DISEASE WITH HYPERTENSION AND ARRHYTHMIA

Case I.—N. S., a married man, fifty-one and a half years old, came under observation in July, 1924, complaining chiefly of palpitation of the heart, weakness, and loss of 70 pounds in weight.

Present History.—The illness began three years ago. At that time he was examined for life insurance and he was turned down because he had high blood-pressure. Previous to that time he had no complaints, but he would get palpitation of the heart and occasional shortness of breath on exertion. He began to lose weight steadily and lost about 70 pounds since the onset. He sleeps pretty well. About a year ago he saw a physician, who, because of his loss in weight, had a complete gastrointestinal x-ray series done for evidence of malignancy of the stomach, but all of the plates were negative. He was also treated by another physician for heart disease, without any benefit. For the last few weeks he has become quite nervous. He has no gastric symptoms, he perspires excessively at times. He has no increased frequency of urine.

Past Illnesses.—He suffered with tonsillitis a good deal as a child and suffered frequently from colds.

Habits.—He was a heavy eater. He used to smoke three strong Havana cigars a day, which he has given up in the last five weeks and now smokes only cigarettes. He does not take alcohol, tea, or coffee.

Family History.—His father died twenty-five years ago of cancer of the stomach. His mother is living. She is about eighty years of age. She has stomach trouble. He has three brothers and three sisters. They are all married and are well. One brother, however, suffers from gastric symptoms.

Examination showed a rather thin, medium statured, middle aged man weighing 135 pounds, with a blood-pressure of 175/85 and a pulse of 110, which was irregular. The skin was smooth, soft, tense, and moist. There was a definite, rapidly appearing *tâche*. There were no areas of generalized pigmentation, there was one pigmented mole on the left chest anteriorly. There was an extensive growth of hair on the skull, over the sternum, on the chest, on the back of the arms and forearms. There were no abnormalities of the skull. The eyes were brown in color. The pupils were round and equal, reacted to light and accommodation, there was no nystagmus. Graefe, Stellwag, Dalrymple, and Kocher signs were all negative. There was marked twitch-

ing of the upper lids and puffiness over both upper and lower lids. The teeth were in rather good condition, there were some gold crowns in the upper set and also on the lower molars. The throat was congested. The neck was long and narrow. The thyroid was palpable and was normal in size and consistency.

The chest was definitely barrel shaped. The lungs were normal. The heart was not enlarged. There were no murmurs. There was a marked arrhythmia and the second aortic sound was accentuated. There was marked flushing of the face during the examination.

The abdomen was scaphoid. There was a marked pulsation of the abdominal aorta with no tenderness, no masses or rigidity felt. The lower border of the stomach was felt a fingerbreadth above the level of the navel. The liver and spleen were not enlarged. The kidneys were not palpable.

The upper extremities were thin. The hands were broad, with a marked fine tremor of the fingers. The lower extremities were thin. There was no edema. There was marked lordosis of the thoracic spine. There was slight epigastric and abdominal adiposity. The genitals were normal. The basal metabolic rate was *plus 57 per cent.*, by the gasometer method.

This patient was evidently suffering from the triad of tachycardia, with arrhythmia and loss of 70 pounds in weight, with a systolic hypertension, for a number of years. Careful examination of the gastro-intestinal tract, as well as the x-ray examination, did not demonstrate any evidence of malignancy. There was no definite evidence of cardiovascular disease. The basal metabolic rate, however, determined the presence of hyperthyroidism. No goiter could be demonstrated. The patient was put to bed for about three weeks and iodine therapy instituted in the form of Lugol's solution, beginning with 1 minim three times a day and gradually increasing every other day. On admission to the hospital his weight was 126 pounds. When he left he had gained $9\frac{1}{2}$ pounds, his tremor had disappeared, his pulse was reduced to 90. Lugol's solution was gradually increased to 25 minims and he was sent to a high altitude and kept

on iodine therapy all that time. The following records will indicate the improvement:

July 14, 1924.—Weight 142 pounds. Pulse 96. Blood-pressure 165/75.

July 18, 1924.—Basal metabolism *plus 32 per cent.*

August 25, 1924.—Now taking Lugol's solution 25 minims; feels fine; no palpitation of the heart, weight 166½ pounds, pulse 92, blood-pressure 155/90, cardiac irregularity gone.

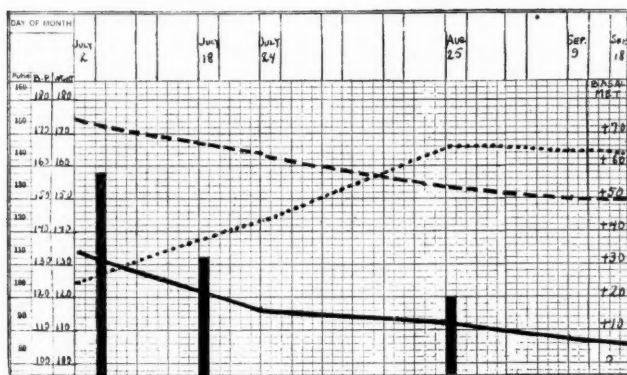


Fig. 113.—Showing the effect of Lugol's solution on the pulse, blood-pressure, basal metabolism, and weight in Case I.

- pulse.
- - - blood-pressure.
- ... weight.
- basal metabolism.

September 2, 1924.—Feeling fine; gaining steadily in weight; weight 162 pounds; pulse 90; blood-pressure 158/68.

September 9, 1924.—Pulse 88, weight 160 pounds, blood-pressure 140/85, cardiac arrhythmia gone, basal metabolism plus 14 per cent.

This patient demonstrates the efficacy of Lugol's solution in relieving the cardiovascular symptoms (Fig. 113).

A CASE OF TINNITUS WITH CARDIOVASCULAR SYMPTOMS OF
HYPERTHYROIDISM

Case II.—B. C., a middle-aged man of forty-eight years, came under observation in April, 1925 complaining chiefly of tinnitus and difficulty in hearing.

Present History.—About a year ago, while in swimming, he suddenly felt weak and felt that all his energy was giving out and he swam ashore with difficulty. Following that incident he began to suffer with palpitation of the heart and ringing in the ears, with head noises. He began to lose rapidly in weight and lost about 32 pounds (from 180 to 148 pounds) in about three months. He began to have pains in the shoulders and the left knee at times, and he became exceedingly nervous. On account of the pains he was advised to see a laryngologist, who took out his tonsils, and except for occasional pains in the left knee the pains were relieved. He suffered a great deal from sleeplessness and tossed about at night. Ever since the onset he noticed a marked shaking of his hands and feet. He has palpitation of the heart, but no dyspnea. The tinnitus had been growing steadily worse and this is now his chief symptom. The ears were examined and proved to be normal.

Past Illnesses.—He suffered a great deal from colds and tonsillitis as a child, but he had no other illnesses. His urine at one time showed 1/10 of 1 per cent. of sugar, but this had cleared up and sugar tolerance tests were all normal.

Habits.—He was fond of sweets. He has given up smoking on account of his condition. He lives a great deal on vegetables and takes no alcoholic liquors.

Family History.—His father died at the age of thirty-three; he had a throat trouble which was probably cancer. His mother died at the age of sixty of pneumonia. He has one brother and two sisters, both of whom are well, except that one sister shows a tendency to obesity.

Examination showed a dark complexioned, rather plethoric, broad statured, middle aged man weighing 156 pounds, 5 feet, 7 inches in height. His pulse was 108 and his blood-pressure was 195/85. His skin was smooth; there was a marked *tâche*. There

was no general pigmentation except for a few scattered pigmented spots in the epigastrium and one on the chest. There was an extensive growth of axillary hair and hair over the front of the chest, the sternum, shoulders, and back. The pubic hair merged with the lower abdominal hair, which was very extensive. There were no abnormalities of the skull. The face was rather plethoric. The eyes were rather prominent. The palpebral fissures were of medium width. The eyes were blue in color; the pupils were round and equal, reacted to light and accommodation, with no nystagmus. Graefe, Stellwag, Dalrymple, and Kocher signs were all negative. The teeth were rather broad and square and long. There was no evidence of decay. The throat was congested. The tonsils were absent, having been removed. The neck was long and broad. The thyroid was not distinctly palpable and there were no abnormalities.

The chest was very long with a wide costal angle. The mediastinal area of dulness was $7\frac{1}{2}$ cm. The heart was normal in size. There were no murmurs; it was regular but rapid; the second aortic sound was accentuated. The abdomen was somewhat distended. There were no areas of tenderness, masses, or rigidity felt. There was considerable distention of the stomach and the colon. The lower border of the stomach was felt at about a fingerbreadth above the level of the navel. The liver and spleen were not enlarged. The kidneys were not palpable. The upper extremities were normal. The hands were rather broad. There was a very marked fine tremor of the fingers. The lower extremities were well developed. There was a moderate amount of adiposity, confined principally to the lower part of the abdomen, the epigastrium. The urine examination was normal. The specific gravity was about 1018. The blood-sugar was 0.100. Three basal metabolism tests were performed, each by the gasometer method, and they showed respectively *plus 34*, *plus 31* and *plus 30 per cent*.

The patient was put on iodine in the form of Lugol's solution, beginning with 1 minim twice a day, and increasing the dose by 1 minim every week. The following records indicate the improvement in the condition:

April 19, 1925.—Weight 162 pounds, pulse 108, blood-pressure 195/85.

April 27, 1925.—Feels a great deal better, the noises are much less than they were, and he thinks the nervousness has improved.

April 27, 1925.—Weight 168 pounds, pulse 98, blood-pressure 170/80, now taking Lugol's 4 minims, twice a day. His general condition is much better. He still has a moderate amount of tinnitus and tremors of the fingers.

May 5, 1925.—Weight 173 pounds, pulse 90, blood-pressure 175/100.

May 11, 1925.—Feeling better. The ringing in the ears is much improved. He has no palpitation of the heart. He sleeps well. His weight is $175\frac{1}{2}$ pounds. His pulse is 84 and his blood-pressure is 155/70.

May 18, 1925.—The ringing in the ears has subsided. He is improving gradually. His weight is $178\frac{1}{2}$ pounds. His pulse is 84 and his blood-pressure is 150/80. He is now taking Lugol's solution, 6 minims.

May 25, 1925.—All the symptoms have improved. The tinnitus is very slight. He is gaining steadily in weight. He sleeps well. He has no palpitation of the heart. His weight is $181\frac{1}{2}$ pounds, his pulse 90, and blood-pressure 140/90.

June 1, 1925.—He feels fine; the tinnitus has entirely disappeared; he sleeps well; he has no palpitation of the heart. His weight is 180 pounds, his pulse is 82, and his blood-pressure is 140/70.

June 8, 1925.—His weight is 179 pounds, his pulse 86, and his blood-pressure is 140/90. He is feeling fine. His basal metabolic rate is *plus 14 per cent.*

June 15, 1925.—He feels fine; his tinnitus has entirely gone; he is steadily gaining in weight; he has no palpitation and no tremor. His weight is 179 pounds. His pulse is 88 and his blood-pressure 145/75. He is now taking Lugol's solution, 8 minims, twice a day.

This patient was suffering from marked tinnitus, palpitation and rapid loss in weight, and sleeplessness. Because of the

tinnitus and indefinite pains, he had been treated for his nose and throat condition, with relief from the pains, but no change in the tinnitus. The tinnitus was probably a vasomotor symptom as the result of his hyperthyroidism, which was demonstrated by the basal metabolic rate of plus 34 per cent. There was no evidence of any thyroid enlargement. The symptoms were essentially vascular, and the prompt improvement under Lugol's solution strongly suggested hyperthyroidism as the causative factor (Fig. 114).

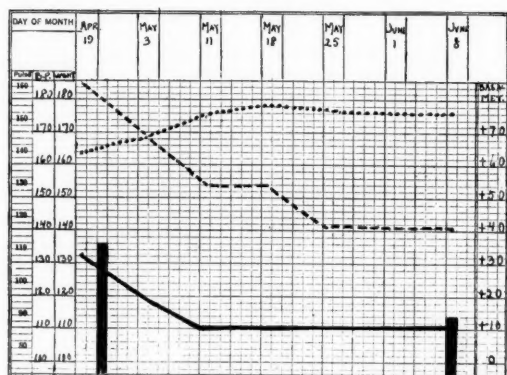


Fig. 114.—Showing the effect of Lugol's solution on the pulse, blood-pressure basal metabolism, and weight in Case II.

- pulse.
- - - blood-pressure.
- ... weight.
- basal metabolism.

A CASE OF HYPERTHYROIDISM WITH CARDIOVASCULAR SYMPTOMS IN A YOUNG MAN, SIMULATING ACUTE ENDOCARDITIS

Case III.—K. E. S., a young man thirty years of age, married, was seen once in February, 1924. He is under treatment by his family physician in Connecticut. He complained chiefly of palpitation of the heart.

Present History.—Just before Christmas he passed a life insurance examination. In the early part of January he went

South. While there he began to suffer with intense palpitation of the heart and his pulse was around 108. The pulse gradually increased to 122. Since that time the palpitation was constant and his pulse varies from 108 to 150 or 160 and is irregular at times. He has grown gradually more nervous and lost 35 pounds in weight. He suffered a great deal from constipation. He always perspired excessively and was always of a nervous temperament. Since the onset of the illness he was given bromids and digitalis. He took both without much benefit and no change in the palpitation, but he did notice that when he took the bromids he became somewhat less nervous. He attributed the onset of his illness to an attack of ptomain poisoning which both he and his wife developed as the result of eating chili con carne. He always suffered a good deal with gas in the stomach, but he never had any actual pain. He vomited pretty regularly since the onset, but he attributes it to having taken digitalis for a long time. He was in the army for eighteen months and was on three fronts. He thinks the tension of the army service probably brought on his nervousness. He always suffered with attacks of migraine. While South it was thought that he had endocarditis, which was due to infected teeth. He had the infected teeth removed, without any benefit.

Past Illnesses.—He had scarlet fever many years ago and also had an attack of appendicitis. Fifteen years ago he suffered from blood poisoning.

Habits.—The patient prefers red meats. He smokes twenty cigarettes a day, but he cut them down to ten since the onset of his illness. He found that smoking did not seem to affect his heart. He hasn't taken alcoholic liquors for the last five years.

Family History.—His father is alive and well. He is seventy-four, rather thin, and has always been nervous. His mother is living. She has always been nervous. She has a goiter. He has no brothers and no sisters.

Examination showed the following: The patient is an exceptionally tall, thin, highly nervous, dark complexioned young man with generalized tremors. He weighs 161½ pounds, and is

6 feet, $1\frac{3}{4}$ inches tall. His skin was smooth, soft, strikingly velvety, almost feminine in type, with a marked tache. There was no evidence of generalized pigmentation except for a few small pigmented areas on the back of the arms. The scalp was covered with fine, silky, black hair. The eyebrows were very thick. There was a thick growth of hair on the front of the chest, extending downward. The pubic hair had a straight border. There was a moderate growth of hair on the lower half of the thighs and on the back of the forearms. The face was long and thin. The palpebral fissures were rather wide. There was a suggestive exophthalmos. The eyes were brown in color. The pupils were round and equal, reacted to light and accommodation. Graefe, Stellwag, Dalrymple, and Kocher signs were all negative. The teeth were in excellent condition. There was considerable secretion of pus at the roots of the teeth. The neck was long and narrow. The thyroid was distinctly palpable, normal in consistency, and not enlarged.

The chest was long and narrow, with an acute costal angle. The lungs and heart were normal, except for marked tachycardia.

The abdomen was rather soft, and somewhat distended. There was a laparotomy incision on the right side about an inch above the navel. There was a smaller one about 2 inches to the right of that. There was a small postoperative hernia. The lower border of the stomach could be felt above the level of the crest of the ilium. The liver and spleen were not enlarged, the kidneys were not palpable. The genitals were normal. The extremities were very thin. The hands were long and narrow and there was a marked tremor of the hands. There was notable absence of adiposity. The basal metabolic rate by the gasometer method was *plus 68 per cent*.

This patient, who suddenly developed tachycardia, was considered as a case of acute endocarditis. There was no history of rheumatic fever. The removal of a possible focal infection in the teeth made no impression on his condition, nor did the administration of digitalis. The association, however, of the tachycardia, loss in weight, asthenia, with a marked increased basal metabolic rate, definitely established the diagnosis of

hyperthyroidism, although there was no appreciable enlargement of the thyroid.

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CLINIC OF DR. HYMEN R. MILLER

POST-GRADUATE AND MONTEFIORE HOSPITALS

SCLEROSIS OF THE PULMONARY ARTERY AND ITS BRANCHES¹

It is possible to recognize sclerosis of the pulmonary arteries and its branches as a fairly well-defined clinical condition. It has been reported by many observers, the clinical diagnosis corroborated at autopsy. On the other hand, not seldom autopsy findings alone have revealed the condition. A study of autopsy records discloses patients in whom there is sclerosis of the pulmonary artery and its branches and no discernible sclerosis elsewhere in the body. These cases are comparatively few in number.² More often the pathologist encounters pulmonary artery sclerosis in patients who have marked general arteriosclerosis, and in this connection it is of interest to note

¹ The expenses of this investigation were defrayed by the Rosa Rossbach Memorial Fund.

² Most writers on the subject of pulmonary vessel sclerosis have not attempted to separate atherosclerosis of the lung vessels as an entity *sui generis*. The literature contains a goodly number of articles nearly all of which deal with these vessel changes as part of the general system vessel alterations, or as related to disorders of the lung, pleura, or heart. However, there are observers who describe cases of so-called primary pulmonary vessel sclerosis (Aust, Crudelli,³ Eppinger and Wagner, Giroux, Kidd,³ Klob,³ Kitamura,⁴ Ljungdahl, Laubry, Mönckeberg, Rogers, Rossel, Romberg, Sanders, Tugendreich, Wolfram, and Wodynski). The primary malady consists of an obliterating endarteritis of the smaller radicles. There is intimal thickening, hypertrophy of the muscle layer, but calcification is not frequent. At autopsy lungs, heart, systemic vessels are uninvolved, emphysema and mitral stenosis are conspicuously absent. The early period of adult life exhibits a greater incidence for this process; there are no concomitant signs or symptoms attributable to any disease outside the lung vessel impairment.

³ Cited by Eppinger and Wagner.

⁴ Quoted by Warthin in contribution to Med. and Biol. Res., vol. 2, 1909.

that a large percentage of general autopsies shows systemic arteriosclerosis and no sclerotic involvement in the pulmonary system.

Some have sought to explain the sclerosis in the pulmonary arteries as a specialized process caused by infection, or produced by mechanical factors which directly increase the blood-pressure in the pulmonary arteries. Still other observers maintain, effectively, that the same degenerative process seen in arteriosclerosis of the aorta and other systemic vessels is responsible for the sclerosis in the pulmonary vessels. This consists of a fibrotic change in the walls of the vessels, the intima being most frequently involved, and at times the media and the adventitia. The lesion may be irregularly sprinkled throughout the pulmonary artery and its arborization, or it may be continuous, involving a single portion or practically the entire extent of the pulmonary artery system. At some future time we shall report upon the pathologic study of the cases in which the process is confined to the pulmonary arteries alone, and also of those wherein the condition is found with general arteriosclerosis, and the attempt will be made to ascertain whether the disease is identical in each instance. In this paper our object is to relate briefly the anatomic and physiologic items which have a clinical interest in the consideration of pulmonary artery sclerosis and to describe the etiologic factors and the striking symptomologic picture and its differential diagnosis.

ANATOMY

In its relative corresponding situation in the chest and in its function the pulmonary artery appears to resemble the aorta, yet there are striking differences in the comparison. Both vessels seem similar in structure macroscopically; each vessel serves as an exit channel for the blood mass leaving its ventricle, and each is guarded by semilunar valve segments. However, since the aorta has to deliver its blood into a large systemic circulation, while the pulmonary artery pours its blood into a comparatively small circuit, the blood-pressure in each vessel will be different, also the required propulsive force at the mouth

of each vessel. Structurally, there are disparities, too, between the aorta and the pulmonary artery; the latter is of finer texture and there is no medial thickening about the Arantii bodies in the adult; the pulmonary artery has a thinner wall and the ring formation around its valve is not so definitely formed as in the aortic valve. The left ventricle whence the aorta springs is considerably thicker and more powerful than the conus arteriosus of the right ventricle. It is obvious that the pulmonary artery is not intended to withstand the same degree of pressure which exists within the aorta. The pressure in the right side of the heart is appreciably less than that in the left side of the heart; moreover, the range and shift of pressure changes are less marked in the smaller (pulmonary circulation) than in the general systemic circulation. Because of its more delicate architecture the pulmonary artery, more so than the aorta, is likelier to dilate earlier and to a greater degree.

The lesser circulation exists between the right ventricle and the left auricle. It comprises the pulmonary artery, its two branches with their terminal ramifications, which as pulmonary capillaries form plexuses lying directly beneath the respiratory epithelium and the walls and septa of the alveoli of the lung parenchyma. A single layer of capillary structure lies in the septa separating the alveoli. The return flow of blood from the lungs begins in the pulmonary capillary veins, gradually broadening into larger branches to form the four large pulmonary veins which empty into the left auricle of the heart. Throughout their course the veins, the small radicles, the larger branches interbranch freely. The lesser (pulmonary) circulation, therefore, consists of a mass of intercommunicating vessels.

The pulmonary artery carries the large volume of unoxygenated blood from the right ventricle to the lungs. The vessel is wide, short, about 5 cm. long, and 30 mm. in diameter. The right pulmonary artery branch is larger and longer than the left. At the root of the right lung it is divided into two branches, the larger, lower branch supplies the middle and lower lobes of the right lung, while the smaller and upper branch goes to the upper lobe. The left pulmonary artery also travels in a hori-

zontal direction to the right lobe of the left lung, and is smaller and shorter than the right branch. At the root it divides into two branches, one for each lobe.

PHYSIOLOGY

Blood is pumped from the right ventricle into the pulmonary artery; the blood-pressure in the artery will be higher than that in the capillaries because of the peripheral resistance in the latter, and because the artery is closer to the propulsive force of the right ventricle. As we near the left auricle, away from the right ventricle, the pressure decreases; naturally in the capillaries the pressure will be higher than in the pulmonary veins. The peripheral resistance in the pulmonary circulation is much less than in the systemic system and, accordingly, as a corollary, the blood-pressure in the pulmonary artery is distinctly less than in the aortic system. There is a vast lung capillary network, and, as a consequence, the velocity of flow through this bed is greater than in the systemic capillaries. We have, therefore, in the pulmonary circulation, as compared with the systemic, a distinctly lower blood-pressure and a distinctly greater velocity flow. The mean pressure of the pulmonary artery, for instance, is one-seventh of the mean pressure in the aorta, 15 to 20 mm. Hg.¹ Since less power is required to maintain the pulmonary circulation, we are not surprised to note the comparative thinness and muscular inefficiency of the right ventricle as compared with the left ventricle.

In addition to the laws of hydraulics which control the flow of blood through the pulmonary circuit, there is the influence of respiration. The lungs, normally in a state of overdistention, have a constant tendency to recoil and collapse. The force with which they tend to collapse is directly indicated by the negative pressure in the pleural cavity, -6 mm. Hg. During inspiration the lungs become more distended and the negative pressure in the pleura is greater, reaching -30 mm. Hg. The

¹ Physiologists differ about the exact blood-pressure figures in the pulmonary circulation. The figure cited is from Starling's *Human Physiology*, 1920.

negative pressure in the pleura (-6 mm. Hg. at the end of inspiration and -30 mm. Hg. during forcible inspiration) transmits its effect upon the heart and the great vessels in the thorax. In the neck and in the abdomen the vessels are subjected to positive pressure. The blood will move from the positive pressure regions to the thorax where the pressure is negative, so that the negative pressure in the thorax serves to suck and draw blood into the chest. The yielding, thin-walled veins will be much more affected by the negative pressure than the comparatively thick non-distensible arteries. The negative pressure of the pleural cavities acts to enhance the flow of blood from the veins into the heart, not interfering with the arterial outflow of the heart's blood. Since, during inspiration, the negative pressure is greater, the heart will receive a greater supply of blood during inspiration, and thus the arterial blood-pressure will be greater during inspiration.

The structure and dynamics of the lesser circulation have important bearing in the clinical appreciation of pulmonary vessel sclerosis.

ETIOLOGY

From our brief review of the physiology and anatomy it is apparent that the pulmonary artery system represents a conduit for blood extending from the conus arteriosus of the right ventricle to the mitral valve in the left side of the heart. Obviously, an interference or obstruction of blood flow in the pulmonary system can produce heightened blood-pressure within this system, and dilatation of the walls of the artery with subsequent pathologic thickening. The most usual site for obstruction is the mitral valve. Mitral stenosis is a frequent accompaniment in pulmonary sclerosis. In mitral stenosis the condition of back pressure is distributed over the greatest possible extent of the pulmonary arterial bed, inasmuch as the obstruction to blood flow takes place at the very exit of the system. There is, also, the added factor of resultant lung congestion induced by scant emptying of the left auricle, its early stretching, its ineffectual hypertrophy in its attempt to overcome its engorgement. And yet mitral stenosis can be found, though extremely

rarely (see Table 4), in patients who have general arteriosclerosis and in whom the pulmonary circulation is spared. That this mechanical obstruction is an important element in the production of pulmonary arteriosclerosis is nevertheless likely, for that matter, obstruction anywhere in the lesser circulation. We may find the obstruction congenital or acquired. Under the acquired causes, the block may exist in the pulmonary veins, within the pulmonary vessel bed as in general pulmonary arteriosclerosis, in any of the large branches, in pulmonary arteritis (luetic, Ayerza's disease), in pulmonary valve insufficiency, in acquired pulmonary artery—aorta aneurysmal involvement, in obstruction from pathologic processes in the lungs, *i. e.*, emphysema, or pulmonary venous congestion, etc., in mediastinitis. Congenitally, there may be coarctation of the aorta, hypoplasia of the aorta, an inadequately developed right ventricle, or narrowing of the pulmonary veins.¹

Whatever the cause of block, eventually the lesser pulmonary circulation engorges and suffers because the left ventricle grows ineffective to maintain the essential balance of pressure between the right and left sides of the heart. As a result the unopposed force of the right side of the heart permits lung vessel engorgement to increase, and pathologic changes in the walls of these vessels take place.

A review of the reports of the last 800 cases coming to autopsy at the Montefiore Hospital discloses two groups of cases, *viz.*, a larger group of 41 cases in which pulmonary vessel sclerosis was present, but in which there was also general arteriosclerosis, and a smaller group of 18 cases in which the sclerotic process seemed to be confined to the pulmonary vessels alone. A survey of these 18 cases of pulmonary vessel sclerosis (see Table 2) indicates that the condition was about equally distributed in both sexes, that the age incidence ranged from twelve to fifty-six years (*8 cases were in patients less than twenty-four years old*), that often a lesion was found in the lungs, not always of direct bearing upon the lung vessel sclerosis, and that in fifteen instances the mitral valve was markedly stenosed, only slightly

¹ Burton-Opitz (see Bibliography).

thickened in another case. The relationship of mitral stenosis to pulmonary artery sclerosis we shall discuss more fully. In these cases the histories record no particular infection as a direct causative factor. But this point may not always have been kept in mind by the hospital intern when he obtained the amanuensis. Certainly in Case No. 6 (autopsy No. 3567-A) infections were searched for, since the patient presented symptoms which aroused the suspicion of pulmonary vessel disease. The history¹ of this case is as follows:

H. L., age forty-five, Jewish male, born in Russia, a painter by occupation. He entered Montefiore Hospital in August, 1921, complaining of dyspnea, weakness, cough, pain in the chest upon deep inspiration. His family, personal, and past history yielded little relevant to his present condition. His occupation led to the study of possible plumbism as a factor, but this was not established. Clinically he presented a striking progressively increasing cyanosis, dyspnea, polycythemia, and some curving of his finger nails, but no distinct clubbing. The blood-pressure was 105/70. There was no evidence of syphilis, tuberculosis, or nitrogen retention, and the x-ray studies revealed extensive peribronchial fibrosis, most marked in the left upper lobe, slight hyperaëration of both lung fields, and moderate hilus fibrosis. The x-ray of the heart showed a broadening of the aortic shadow and an increased prominence of the arcus pulmonaris. The patient's condition was rather stationary for a number of months; a clinical notation made about seven months after his admission reads as follows: "No murmurs audible. There is a slight thickening of the radial arteries. Blood shows marked polycythemia. However, there is no true clubbing of the fingers, although nails are curved and cyanotic. The cardiac enlargement, enlarged liver, in the absence of signs of advanced structural emphysema, suggest the possibility of sclerosis of the smaller radicles of the pulmonary artery" (Dr. E. P. Boas).

The laboratory findings were: a negative blood Wassermann reaction, the sputum repeatedly negative for tubercle bacilli, an increase in the number of red blood-cells (8,363,000) and in the percentage of hemoglobin (110 per cent.) with a white cell count of 16,400, of which 75 per cent. were polynuclear cells. The blood chemistry figures were not abnormal. The cyanosis became extreme, assuming a dark muddy gray character; gradually signs of cardiac failure supervened, the patient dying in March, 1922. The autopsy performed ten hours later by Dr. D. P. Secof is given in the following protocol:

Heart: Weighed 320 grams. Epicardial surfaces all over thin, smooth,

¹ For permission to publish this case I am indebted to Dr. B. S. Oppenheimer, Chief of the Medical Service, Montefiore Hospital. Dr. Secof, of the same institution, furnished this autopsy summary, and kindly helped in the procuring of the autopsy records for this paper.

and glistening. There is marked dilatation of right ventricle and auricle. On section, heart muscle glazed, otherwise normal. Right auricle moderately dilated, slightly hypertrophied; right ventricle markedly dilated, moderately hypertrophied. The conus of the pulmonary artery markedly dilated, admitting tips of three fingers. Pulmonary ring stretched. Pulmonary leaflets normal. Tricuspid valve normal. Left ventricle normal size. No abnormalities of mitral or aortic valves. Coronaries negative except for slight yellowish flecking in intima in larger branches. Pulmonary artery dilated, otherwise normal.

Aorta: Small portion obtained shows no abnormalities.

Lungs: *Right*: marked emphysema along medial borders anterior lobes; lower lobe firm, upper lobe shows marked diffuse emphysema and upper third larger, emphysematous blebs up to 2 cm. in diameter. On section the upper lobes are slightly edematous, emphysematous; the lower lobe shows a confluent bronchopneumonia, red stage, the lung tissue dark red, friable, drips blood. Bronchi slightly dilated and injected throughout. Vessels: in larger branches there is slight yellowish flecking of intima, otherwise normal. *Left*: similar in general to right—emphysematous blebs medial border upper lobe, marked emphysema both lobes. Early confluent bronchopneumonia lower lobe. Bronchi and vessels similar to right.

Spleen: Weighs 200 gm. average size and consistency; capsule thin, smooth. On section, pinkish-red surface, smooth. Malpighian bodies and trabeculae average size; here and there small areas of smooth grayish-white up to 3 mm. in diameter.

Kidney: Weighs 220 gm., larger than average, firm. On section, striations regular, in places more prominent than average. Cortex of average width; capsule strips with ease.

Liver (small portion): Shows marked chronic passive congestion and fatty infiltration.

Microscopic Notes.—Heart: Muscle-fibers pale staining, moderate fatty infiltration. Slight increase connective tissue, vessels slightly thickened.

Lung: 1. Marked emphysema. Bronchi markedly thickened. Vessels, marked thickening all coats and hypertrophy of elastic layer.

2. Similar, in addition, diffuse congestion, most marked bronchial walls.

3. Large area of bronchopneumonia, moderate chronic passive congestion. Vessels markedly thickened. Bronchi dilated, walls thickened, and injected.

Liver: Marked congestion, capsule thickened, fibrous.

Spleen: Moderate general increased connective tissue, sinuses dilated, Malpighian bodies large, trabeculae and vessels thickened.

Kidney: Glomeruli slightly shrunken, fibrotic, moderate diffuse congestion.

Anatomic diagnosis: Pulmonary emphysema, emphysematous blebs, hypertrophy and dilatation conus pulmonary artery, dilatation pulmonary artery, marked passive congestion lungs, spleen, kidney, and terminal confluent bronchopneumonia, early.

There was marked dilatation of the pulmonary vessels, from the large stem of the artery extending through its ramification. This may have been an idiopathic widening of the blood-vessels or the end-result of the prolonged and exaggerated emphysema.

The photographs of the microscopic sections from the lung of this patient demonstrate the degree and extent of lung vessel

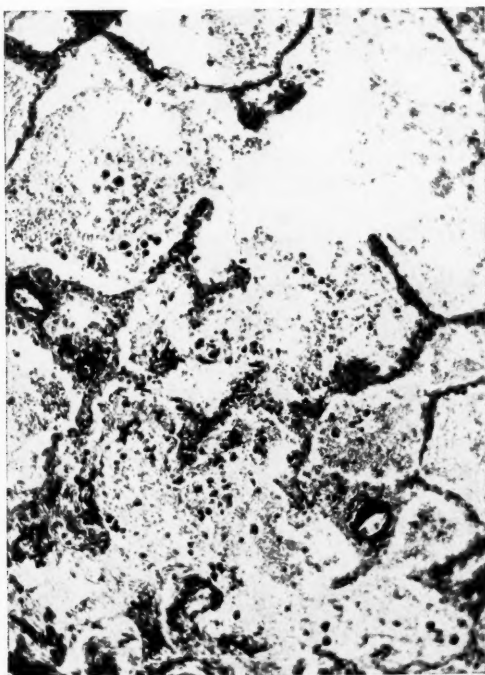


Fig. 115.—Low-power microphotograph showing three small pulmonary blood-vessels, with eccentric thickening of the wall and narrowing of the lumen.

thickening in the smaller radicles, the musculature is probably thickened and the elastic layer lamellated, often in eccentric fashion. Are we to interpret this dilatation and muscular hypertrophy as a specific pathologic entity, or does it represent merely an earlier phase of the similar pathologic process seen in

pulmonary vessel sclerosis where the associated mitral stenosis probably played a telling rôle in the genesis of the atherosclerosis?

That a tightly constricted mitral orifice seemingly contributes in a striking manner toward the evolution of pulmonary vessel

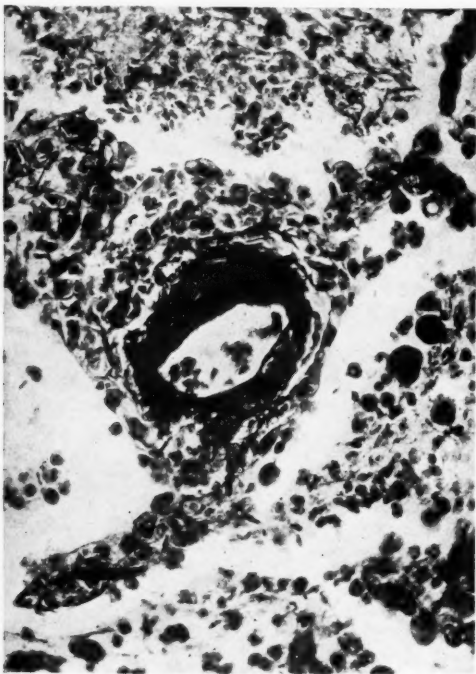


Fig. 116.—A high-power microphotograph of one of the three vessels, from Fig. 115, *i. e.*, the one in the lower corner, corresponding to the number 5 on a watch dial, illustrates the extent of lamellation of the elastic layer.

sclerosis is indicated by the case which follows. (It is reported through the courtesy of Dr. Macpherson and Dr. Shattuck, but is not included in Table 2, since it is but a single report unrelated to a study of the autopsy records from the Post-Graduate Hospital.)



Fig. 117.—A low-power microphotograph of a medium-sized lung vessel, depicting its normal wall and elastic layer. The vessel is of the same magnification and almost of the same caliber as the one shown in Fig. 119. Note the difference. Figures 115–117 are from case H. L. The pathologic vessel lesions were like those published in the so-called primary pulmonary vessel sclerosis, the finer radicles chiefly were affected. Unlike this type of condition, in the case of H. L. there was an emphysema, severe in character. Just what part this emphysema contributed toward the production of lung vessel impairment we cannot estimate. As in primary pulmonary vessel sclerosis, this patient, too, had no mitral stenosis.

The patient, A. P. H., an American Protestant minister, born fifty years ago, entered the private corridor of the Post-Graduate Hospital in May, 1925. He had had repeated attacks of rheumatic fever, the first when twelve years old, the second at the age of fifteen, when he knew that he had heart trouble. For the past ten years his heart would fibrillate. Ten years ago he had pain in his left malar region and four years later he had difficulty from an impacted tooth in the same region. Following the removal of the tooth one year ago he discharged pus. For ten days before his admission to the hospital he had

fever and sweating. Upon physical examination the patient presented signs of basal lung involvement, an enlarged heart that was fibrillating, and had a stenosed mitral valve. He was pale, but had no petechiae. The laboratory examination showed a steadily increasing anemia of a secondary type with a leukocytosis, the figures varied from 7000 to 13,400, the tendency being in most counts toward the higher number with polynucleosis. Several blood-cultures were sterile. The blood chemistry figures were not abnormal. The



Fig. 118.—This is a gross picture of the lung of patient A. P. H., demonstrating sclerotic plaques (intimal) within a large branch of the pulmonary artery.

patient continued his febrile course (from 101.8° to 105° F.) with an occasional chill. A transfusion of blood did not help him rally. He developed a terminal cerebral insult and died July 3, 1925. There was no cyanosis except as part of the very terminal picture. The autopsy was performed one hour after death (I am indebted to Dr. Klemperer for this report) and is as follows:

"Brain: The galea hyperemic, the dura mater tense. The skull from 4 to 5 mm. thick. The vessels at the base of the brain thin walled. In the right arteria cerebri media there is an embolus which adheres to the wall of

the vessel. The right hemisphere is larger and softer than the left and the gyri flattened. On section the left hemisphere is without changes, the right centrum semi-ovale, the nucleus caudatus and lentiformis and the capsula interna softened and hemorrhagic. Middle brain and cerebellum without changes.

"Lungs: Left pleural cavity empty, pleura smooth and shiny. The lung is well aerated and distended. In the upper lobe a small fibrous nodule



Fig. 119.—A low-power microphotograph (of the same magnification as Figs. 115 and 117 of patient H. L.), portraying an extensive grade of sclerosis in the medium-sized vessels, from patient A. P. H., the intima is thickened, and the elastic layer lamellated. A comparison with Figs. 115 and 117 of H. L. (where mitral stenosis did not exist) establishes the fact that in A. P. H. (where mitral stenosis was present) the larger and medium-sized vessels were assailed, while in H. L. the pathologic process was confined to the lungs' finer radicles, the larger vessels escaping alteration.

the size of a pea. On section pus can be pressed out from the bronchi of the lower lobe.

"Right lung: The lower lobe adherent to the diaphragm, about 50 c.c. yellow fluid in the pleural cavity, the lower lobe compressed. Pleura smooth and shiny. On the surface of the lower lobe a harder brownish nodule prom-

inent. On section the smaller branches of the pulmonary artery plugged with emboli. The nodule in the lower lobe well circumscribed, brownish, wedge shaped. The lung tissue is not aerated, tough. The large branches of the pulmonary artery show numerous yellow patches.

"Heart: The pericardial sac contains about 20 c.c. turbid yellow fluid. The surface of the heart markedly red. The heart markedly enlarged in both ventricles. The left ventricle forms the apex; it is round. The left auricle distended, its wall thickened, within the lumen a large spheroid thrombus which adheres by a pedicle to the wall. The mitral valve is thickened, the chorda tendinea shortened. The ostium allows only one finger to pass. The aortic valves are retracted, the free margin thickened, and there are verrucæ adherent on the surface. The right and medial valves are fused. The sinus valsalvæ contain calcareous deposits. Tricuspid valve shows thickened and shortened chordæ tendineæ. Pulmonary valves without changes. The septum ventriculorum shows an area of yellowish-red discoloration beneath the septum fibrosum. On section it appears yellowish-red mottled. In the posterior wall of the left ventricle an area of older myomalacia. The coronary arteries show numerous yellow plaques, the aorta is smooth.

"Spleen: This is normal in size. The capsule is smooth. In the center one scar, at the lower pole of the spleen an anemic infarct the size of a cherry. The spleen, on section, is red, with increase of fibrous tissue.

"Liver: The liver is normal in size, Glisson's capsule is smooth. On section it is brownish-red. The lobular markings are distinct. Gall-bladder is filled with green bile.

"Diagnosis: Stenosis of the left auriculoventricular and ventriculo-arterial ostium. Insufficiency of the mitral and aortic valves resulting from chronic endocarditis. Recurrent endocarditis and calcification of the aortic valves. Insufficiency of the tricuspid valve. Thrombosis of the left auricle. Acute myomalacia of the left ventricle. Arteriosclerosis of the coronary arteries and pulmonary arteries. Embolism of arteria cerebri media dextra. Encephalomalacia rubra of the right hemisphere (including capsula interna, nucleus caudatus and lentiformis). Multiple recent and old infarcts of spleen and kidney. Hemorrhagic infarct of right lower lobe of lung. Pleuritic exudate in right pleural cavity with compression and adhesions of right lower lobe. Chronic emphysema of both lungs and chronic purulent bronchitis of both lower lobes. Venæ stasis of lower ileum.

"Comment: In the light of the histologic examination of the heart muscle with the findings of Aschoff bodies in great numbers, the case can be conceived of as a case of recurrent rheumatic endocarditis. The embolism most probably is derived from the thrombosis of the left auricle. There is no macroscopic or microscopic evidence of a superimposed bacterial endocarditis."

This patient had heart disease for nearly forty years. His recent bacterial endocarditis engrafted upon a rheumatic heart bore no relation to his pulmonary atherosclerosis, but the presence of the old stenosed mitral valve is significant.

In Table 1 we note 37 patients who had mitral stenosis during life with clinical signs and symptoms, whose autopsies did not

TABLE 1
THIRTY-SEVEN CASES OF MITRAL STENOSIS UNASSOCIATED WITH PULMONARY
VESSEL SCLEROSIS OR GENERAL ARTERIOSCLEROSIS

No. of cases.	Age incidence.					Sex.		Remarks.
	10 to 20 years.	20 to 30 years.	30 to 40 years.	40 to 50 years.	50 to 60 years.	Male.	Fe- male.	
37	13 cases	7 cases	8 cases	6 cases	3 cases	19	18	The clinical evidence (history, signs, symptoms) indicates that these cases were practically all rheumatic in nature, and that the mitral lesion had existed anywhere from four months to thirteen years.

bare any blood-vessel sclerosis in the general or lesser circuits. These cases were chiefly of comparatively young people, the lesion had existed many years in most of them, and the span of life had been shortened apparently. The sexes were about equally represented, the etiology practically, always, of a rheumatic nature. Among 800 autopsy records, then, there were 37 cases of mitral stenosis unassociated with vessel sclerosis. Evidently, a tightened mitral opening, of itself, is not a frequent cause of pulmonary vessel sclerosis; it failed to produce pulmonary vessel sclerosis in 37 cases. We may assume, perhaps, that these 37 people did not live long enough to enter the middle and advanced years of life during which time blood-vessel sclerosis is wont to develop. On the other hand, inasmuch as mitral stenosis was discovered fifteen times in a small series of 18 cases with pulmonary vessel sclerosis, we may postulate a causal interrelationship between these two conditions. It may not be far fetched to imply that in this small group of 18 cases there may have already existed an "anlage" defect in the architecture of the lungs' blood channels and that the acquired valve closure enacted its mechanical disturbances, causing hypertension in a congenitally vulnerable vascular system with pulmonary atherosclerosis as a final result. These cases,

TABLE 2

EIGHTEEN CASES OF PULMONARY VESSEL SCLEROSIS WITHOUT GENERAL ARTERIOSCLEROSIS

Autopsy number.	Age.	Sex.	Pulmonary artery changes.	Mitral stenosis.	Lungs.
3029	18	F.	Large vessels thickened.	Present.	Interstitial pneumonia.
3030	44	F.	Early atheroma.	Present.	
3064	23	M.	Atheroma patches.	Present.	Old healed tuberculosis.
3142	13	F.	Atheroma.	Present.	Chronic passive congestion.
3260	41	F.	Irregular thickening of large vessels.	Present.	Chronic passive congestion.
3567-A	45	M.	Dilated conus; vessels thick, especially elastic layer.	Absent.	Emphysema; chronic bronchitis.
3355	12	M.	Atheroma patches.	Present.	
3662	39	F.	Intima moderately thickened; sclerosis of root vessels.	Present.	
3663-A	17		Moderate thickening of vessels.	Present.	Infarcts.
3668	58	M.	Moderate thickening of root vessels.	Present.	Emphysema; old healed tuberculosis of apices.
3670-A	44	M.	Moderate thickening of root vessels.	Present.	Emphysema; bronchitis; chronic passive congestion.
3680-A	54	M.	Moderate thickening of root vessels.	Present.	Emphysema; chronic passive congestion.
3682	49	M.	Intima atheroma; conus dilated and hypertrophied; pulmonary artery dilated and hypertrophied	Absent.	Emphysema; asthma.
3736-B	44	F.	Vessels thickened and dilated.	Present.	
3743	56	M.	Vessels thickened and dilated.	Present.	Infarcts; chronic congestion.
3752-C	18	F.	Early atheroma.	Slight thickening of mitral valve.	Infarcts; chronic passive congestion.
3754-A	15	F.	Marked thickening; conus thickened.	Present.	
3760	23	F.	Moderate thickening; conus thickened.	Present.	

Of these 18 cases showing sclerotic changes in the pulmonary arteries, 15 exhibited mitral stenosis; 1 case had slight thickening of the valve. Pulmonary atherosclerosis here seems to occur in the comparative youth of life.

therefore, may stand as an exquisite example of the influence of an elevated blood-pressure operating within the blood-vessels of a closed lung circulation.¹

As is well known, pulmonary artery sclerosis occurs with sclerosis in other parts of the arterial system. An attempt was made to correlate the arteriosclerotic changes in the cerebral, coronary, renal, and extremity vessels with the occurrence of arteriosclerosis in the lung vessels. This is seen in Table 3,

TABLE 3

FORTY-ONE CASES OF PULMONARY VESSEL SCLEROSIS IN PATIENTS WITH GENERAL ARTERIOSCLEROSIS

No. of cases.	Age incidence.	Sex.		Arteriosclerosis involving				Mitral stenosis.
		Male.	Female.	Coronaries.	Kidneys.	Aorta.	Cerebral.	
41	Seventeen to ninety-one years (1 case seventeen years; 1 case eighteen years), others all over forty-six years; greatest number at sixty years or over.	22	19	In 37 cases	In 31 cases	In 3 cases	In 3 cases	In 9 cases; also 3 cases of slight thickening of mitral valve.

Of these 41 cases showing general arteriosclerosis plus sclerosis of the pulmonary vessels, 9 had mitral stenosis and 3 cases had slight thickening of the valve.

which consists of 41 cases, of which 9 had mitral stenosis and 3 slight thickening of the valve. In 29 instances there was no involvement of the mitral valve. It may be that the rigidity of the valve in these cases represents but an additional phase of the general sclerotic process going on in the general and pulmonary circulation at the same time. In other words, in a sense we may include the sclerotic process at the mitral valve as part of the sclerosis of the lesser circulation as a whole or as

¹ An experimental study in animals planned to produce hypertension in this shut-in system, by means of an artificially placed obstruction at the mitral opening, might yield knowledge of interest and value for a comprehension of the mechanism of hypertension and its relationship to blood-vessel alterations. Such a study is contemplated for the near future.

part of the general systemic disease even though the left auricle is comparatively spared. Such an interpretation would imply that in these cases the obstruction at the valve contributed little if any to the cause of pulmonary vessel sclerosis. This point of view gains some support since 29 cases in the group revealed advanced general sclerosis with clearly defined sclerotic changes in the pulmonary vessels, the mitral valve remaining unaffected. On the other hand, we cannot exclude the possible, in fact, extremely probable significant influence of an obstructed mitral valve in the genesis of pulmonary artery sclerosis, first, because, as already pointed out, a stenotic mitral valve would serve as a mechanical cause to produce increased pulmonary blood-pressure with consequent pathology in the walls of the lung vessels, and, second, because of the striking association at the autopsy table of pulmonary vessel sclerosis and mitral stenosis. The chart illustrates this latter point, viz.:

Table.	Number of cases.	General arterio-sclerosis.	Pulmonary vessel sclerosis.	Mitral stenosis.
2	18	Absent.	Present.	15 cases.
3	41	Present.	Present.	9 cases.
4	80	Present.	Absent.	1 case.

Table 4 is a résumé of 80 cases of general arterial sclerosis typical in all respects. This table is included because it offers testimony, if any were needed, that in such cases sclerosis of the pulmonary vessels may be absent. In 21 records there is no mention that the pulmonary vessels were studied or considered for sclerosis; in 59 cases they were specifically studied. It is probable that sclerosis of the pulmonary vessels, if encountered in these 21 cases, would have been noted; however, we may assume with safety that in 59 cases the condition of pulmonary vessel sclerosis was not discovered after search. The age incidence was almost similar to that of the group of Table 3, general

arteriosclerosis occurring in well-advanced years, the sexes represented by 33 males and 47 females. Here mitral stenosis was seen in one instance only. Out of 80 cases of advanced arteriosclerosis with no pulmonary vessel sclerosis, mitral stenosis occurred once.

This presents a startling contrast to the frequency of mitral stenosis in pulmonary vessel sclerosis found as an isolated

TABLE 4
EIGHTY CASES OF MARKED GENERAL ARTERIOSCLEROSIS WITHOUT PULMONARY VESSEL SCLEROSIS

No. of cases.	Age incidence.	Sex.		Arteriosclerosis involving							Mitral stenosis.
		M.	F.	Aorta.	Coronaries.	Kidneys.	Cerebral.	Adrenal.	Mesenteric.	Extremities.	
80	Thirty-four to eighty-five years; greatest number of cases between fifty and sixty years.	33	47	In 31 cases	In 45 cases	In 50 cases	In 20 cases	In 2 cases	In 2 cases	In 5 cases	In 1 case

Of these 80 cases of advanced general arteriosclerosis there is no recorded evidence of pulmonary vessel sclerosis. Only one case had mitral stenosis.

pathologic condition, and in pulmonary vessel sclerosis occurring in general arteriosclerotic patients. It seems safe to infer that mitral stenosis is related to the presence and perhaps causation of sclerosis of the lung arteries inasmuch as mitral stenosis was practically always present in pulmonary vessel sclerosis alone (see Table 2), and mitral stenosis was found in about one-quarter of the cases when pulmonary vessel sclerosis was associated with systemic arteriosclerosis (see Table 3), and finally, because in general arteriosclerosis, unassociated with involvement of the lung vessels, mitral stenosis was practically absent (see Table 4).

We may ask the question whether or not general arteriosclerosis has any influence in stemming or preventing the production or development of lung artery sclerosis. Singularly, in this group (*i. e.*, tabulated in Table 4) of elderly people with marked degenerative blood-vessel changes throughout the

body, the pulmonary vessels were spared. It is as if the profound change throughout the entire general arterial tree could not penetrate to the blood-vessels in the smaller circulation carrying on its normal physiology, and this despite the fact that in many instances there was chronic emphysema, chronic bronchitis or lung infarcts, and even heart muscle changes. Such an observation raises the query whether we are dealing with a process or agent sufficiently specific or selective to spare the pulmonary vessels though all other vessels are attacked, or whether these pulmonary vessels escape pathologic change because they are, as it were, outside the circuit in which abnormal fluctuations in velocity and pressure operate. Yet if this is a possibility, why is there pulmonary vessel sclerosis so often found in patients with general arteriosclerosis? Certainly, in patients of long-standing arteriosclerosis, pulmonary vessel sclerosis might be expected to occur, and it does. When present in general sclerosis are they both part and parcel of the same underlying condition, or are they independent and separable conditions?¹

Evans says that the pulmonary artery and its branches resemble closely the architecture of the aorta. The outer coat has an adventitia of loose connective tissue containing few elastic fibers and occasional longitudinal muscle-fibers arranged in bundles. Nutrient vessels are present. Close to the inner border is the media which has many strong elastic fibers circularly arranged, and between them are muscle-fibers in all directions, but principally having a circular direction. He then goes on to quote Torhorst's description as follows: "Along the inner border of this laminated coat is the musculo-elastic layer running longitudinally to the vessel, but whose individual muscle bundles form a network. This musculo-elastic layer also contains elastic fibers, which along its inner borders are aggregated into a denser bundle to form the inner boundary between this layer and the intima proper. The intima, innermost layer, in the main, has a circular direction and consists of connective tissue, but is rich in fine elastic fibrils, giving the appearance often of strong elastic tissue fibers. In small arteries² both musculo-elastic

¹ Combining Tables 3 and 4 we have a total of 121 cases of general arteriosclerosis; of these, 41 also had sclerotic involvement of the pulmonary vessels. The incidence of pulmonary vessel sclerosis in general arteriosclerosis was about 33 per cent.

² A matter of importance is the identification of what is meant by an arteriole (as distinguished from a small artery or capillary) in the lungs and

and connective-tissue layers are thin and weak. Evans is in accord with Torhorst and Ehlers, who state that degenerative changes in the pulmonary artery begin in the musculo-elastic layer, simulating the reaction and change in the aorta described by Jores in 1903. Jores described in this connection two reactions; hyperplastic intimal thickening: (1) involving the musculo-elastic layer and inner elastic lamella, and (2) a regenerative connective tissue increase of the intima, originating in the innermost layer. Both these types of reaction are to be found, according to these authors, in pulmonary arterio-sclerosis.

According to some authors infections¹ play an important rôle in the etiology of this condition. Not only can the pulmonary artery suffer as a sequel to the general circulatory disturbance brought about by infectious diseases, but the infectious agent itself may assail directly the intima of the pulmonary artery. There are thus reported acute cases of ulceration due to Fränkel's diplococcus, to pneumococcus, to typhoid bacillus, to gonococcus, to the infectious agent of variola (3 such cases were reported). The more general rule is to find pulmonary artery sclerosis caused by repeated insults from an infectious process, notably a gonorrheal infection. It is strange, indeed, that only the pulmonary artery and its branches should be singled out by an infectious agent. It is claimed that poly-arthritis and pericarditis may be associated with sclerosis of the pulmonary artery. The vessels here may possibly be attacked by the same infection responsible for the disease in the joints or in the pericardium or, it may be, as in the case of pericarditis,

in all the other organs and tissues of the body, for that matter. Our comprehension of the physiologic forces capable of producing hypertension and blood-vessel alteration within the lesser circulation or greater circulation must rest until there is a unanimity of opinion as to which blood-vessel radicles are primarily affected, and how their altered appearance differs from their normal state.

¹A protracted discussion at this time upon the wisdom of accepting infection as a selective (specific) etiologic factor seems to us futile. It may well be that infection is not a factor at all and that the same type of degenerative change observed in sclerosis of the aorta and its branches occurs also in the sclerosis of the pulmonary artery and its branches. We reserve for a future occasion, when our pathologic studies shall be completed, the detailed consideration of the pathologic changes in the pulmonary artery vessels of the autopsy material in our hands.

that altered circulatory derangement produces blood-pressure disturbances in the pulmonary arteries, causing sclerosis of their walls. Though the French writers hold alcohol as a cause, this is not likely; nor does syphilis play a rôle. (See, however, relation of lues in Ayerza's disease.)

SYMPTOMS

From the foregoing it is obvious that the clinical picture will depend, in large measure, upon the causative or accompanying pathologic features. Pulmonary artery sclerosis frequently follows as a result of these pathologic conditions and so adds materially to the burden placed upon the right heart. Of itself pulmonary artery sclerosis can compromise the function of the right heart. Clinically, therefore, as a rule, we observe symptoms produced by the original condition, *i. e.*, mitral stenosis, emphysema, etc. There is, however, a symptom syndrome which may be recognized, pointing to the existence of pulmonary vessel sclerosis.¹ The concomitant pathologic disturbances of the heart or the lung, though capable of producing confusing clinical symptoms, should not, and may not, interfere with the rather distinct clinical recognition of sclerotic involvement of the pulmonary vessels. If the patient is seen late in the course of the disease when cardiac failure supervenes, it may be impossible to recognize pulmonary vessel disease.

¹ A clinical distinction between primary and secondary pulmonary vessel sclerosis exists. For example, Giroux asserts that cyanosis and dyspnea are more dominant signs in the primary type, while in the secondary cases, initiated by heart or lung disorders, there is a tendency to drowsiness, "they doze everywhere, on a bench, in the midst of a meal, and it is frequently during this somnolent state that they succumb"; a racking cough and profuse expectoration develop in some of these patients. The 5 primary cases published by Eppinger and Wagner had polycythemia, cyanosis, dyspnea, and a characteristic x-ray picture, wherein the lungs failed to show signs of stasis, in contradistinction to the presence of lung stasis from mitral stenosis. Their patients experienced no pulmonary intermittent claudication (as described by Posselt), nor did they have any "heart failure cells" in the sputum. They summarized the salient features of primary pulmonary vessel sclerosis as a disease showing a large right heart with a comparatively small left heart, no lung stasis (absent heart failure cells), a small pulse, impressive cyanosis, marked edema, relatively mild dyspnea, and characteristic x-ray findings.

The condition is a chronic one and the symptoms are slow, gradual in their development, and of long duration. There is a remarkable disparity between the fully developed impressive cyanosis and the comparative mildness of the dyspnea. There is little evidence of sharp cardiac failure, so that we do not generally see edema of the extremities or the accumulation of fluid in the sac cavities. There are very apt to be recurrent attacks of hemoptysis. There is no body wasting, there is no destruction of the blood-cells apparent (no icterus, no skin hemorrhages). The course of the condition is practically afebrile and there is no distinct leukocytosis. Patients complain of deep-rooted chest pain, but without anxiety of death and without typical radiation as in cardiac angina. The disease pursues an ever-increasing and relentless course; in some cases there are remissions of comparative comfort and freedom from pain and hemoptysis, the cyanosis nearly always persists unchanged. In somewhat greater detail the symptoms are as follows:

Hemoptysis.—This symptom is present, particularly in cases with obstruction in the pulmonary circulation, notably in mitral stenosis, and in lung congestion. Dargeins,¹ in 72 cases of "cardiac hemoptysis," had 53 cases of mitral valve disease, of which 27 were stenotic. But in the clinical condition of pulmonary sclerosis from whatever cause hemorrhage from the lungs is likely. The altered and augmented pulmonary pressure can produce pulmonary venous congestion, dilatation and bulging of the capillaries, also varices; these, together with embolization of the pulmonary artery branches and resulting infarcts, may lead to degenerative processes in the walls of the vessels. Hemoptysis may follow as a consequence of these conditions. It is not always necessarily the sclerosis of the pulmonary vessels which produces hemorrhages, but rather the underlying pathologic disturbance responsible eventually for the sclerotic change. However, the hypertension in the pulmonary vessels and the sclerotic degenerative alterations in their walls frequently can give rise to hemoptyses. Clinically, we must bear in mind

¹ Dargeins: Quoted by Posselt, also by Giroux.

heart infections, lung infarctions, pulmonary tuberculosis, purpuras, etc., as conditions for diagnostic differentiation.

Clubbed Fingers.—Posselt maintains that clubbing of the fingers does not, as a rule, accompany this affection, and he advances this fact as a point in differentiation between congenital cardiac condition, etc. It is beyond the province of this paper to discuss in detail the subject of clubbing of the fingers. It would appear that in many cases of long-standing infection clubbing of the fingers can occur. Thus, for instance, Locke reported 144 cases in which 113 had lung conditions (with infections), 6 had heart conditions, and 11 had alimentary tract lesions (6 of these were biliary cirrhosis). In connection with the lung cases clubbing was noted most frequently in lung infections (bronchiectasis) of the lower lobes. The factor of drainage may be important here. Pathologically, the clubbing represents a slow, progressive bone-forming periostitis, involving not only the terminal phalanges, but the skeleton in other parts of the body; in fact the joints also may show erosion of the cartilages, thickening of the synovial membranes and perhaps effusion, while soft parts are likely to become hypertrophic.

This type of clubbed fingers is known as hypertrophic pulmonary osteo-arthritis and represents a permanent bony change. Such is not the case in simple clubbing of the fingers. The latter condition is apt to disappear upon the elimination of the culpable infectious focus in the body. However, even in so-called simple clubbing, Locke found definite bone change in 12 out of 39 cases. In pulmonary arteriosclerosis there may be an occasional instance of simple clubbing, indicating involvement of the soft parts, but the bone is spared. There may be a ranging degree of cyanosis of the finger-tips, but hypertrophic pulmonary osteo-arthritis is not found.

Cyanosis is a prominent feature and an early one. The face (ears, nose, lips), buccal mucous membranes, also the eye-grounds can become plum colored, the limbs almost of the same hue, as the disease in the lungs lasts or develops. It is well to remember that a mild or even well-advanced degree of cyanosis may be due to the primary cause of the pulmonary sclerosis, thus cy-

anosis may accompany the mitral stenosis, pericarditis, pleuritis, or postinfectious myocardial degenerative processes, or polycythemia (relative). In pulmonary vessel sclerosis the grade of cyanosis may be extreme. This finding is striking because with it there may be no evidence of acute cardiac failure or pulmonary stasis with its usual train of signs, such as edema of the limbs, hydrothorax, ascitis, etc. The cyanosis is greater over the upper part of the body, particularly in the face, neck and upper thorax, and fingers. Paroxysms of alarming cyanosis can take place, sometimes accompanied by transient hemoptyses and attacks of deep-rooted chest pain.

Dyspnea, generally, is not a prominent sign or symptom. As for cyanosis, so too with dyspnea, the primary cause of the lung or heart disease may be the underlying cause. Emphysema may be a chief contributing cause. In pulmonary vessel sclerosis the loss of elasticity and the progressive rigidity of even the smallest vessels prevent the proper exchange of normal gases; this interferes with the normal effect of respiration upon the pulmonary blood circulation. The carbon dioxid content of the blood and its effect upon the respiratory center, accordingly, have important bearing upon the dyspnea, but, in addition, we have to consider the mechanics of the circulatory system with its hypertrophy of the right ventricle, the augmented pulmonary blood-pressure, the increased venous pressure, the hampered respiratory mechanism, and the deranged physiology following these factors. Moreover, a polycythemia or, better, erythremia is likely to be present. This possibly means a greater oxygen-carrying capacity in the blood-stream because of the increased number of erythrocytes. Despite the marked change in actual mechanics of circulation, with its likely resultant physical derangement, dyspnea remains not a significant finding, and this, too, in the face of striking cyanosis. In other words, we are dealing with a situation where a well-advanced cyanosis is seemingly out of proportion and therefore preponderant to a mild type of dyspnea and to the absence or mild degree of stasis present. The respirations are not increased; there is no change in the type of respiration, *i. e.*, no Cheyne-Stokes or Biot character.

Pain.—It is known that in coronary sclerosis, for instance, there may be pain, that sclerosis of the abdominal vessels can cause pain (Ortner), that the peripheral vessels of the extremities may produce pain (intermittent claudication), but the mechanism of pain in these conditions is not clear; nor is its significance and origin understood in pulmonary arteriosclerosis. In sclerosis of the pulmonary vessels stenocardia is not present. If aortic disease is responsible for substernal pain, we have no evidence to support any similar view that sclerosis of the pulmonary artery, at any corresponding site, may produce a similar type of pain. Although the exact localization of the site of pain is not determined, pain is not a rare complaint in pulmonary vessel sclerosis; it may be intermittent and severe. The radiation is apt to be toward the upper part of the chest, and with it there is a sensation of deep-seated though ill-defined distress within the lungs themselves. The pain is paroxysmal, its spread quite limited. There is no anxiety picture as in coronary disease attacks.

DIAGNOSIS

We may expect to recognize pulmonary vessel sclerosis as a chronic, fairly well-defined clinical entity, but it is not surprising to meet a variety of conditions possessing signs and symptoms, as in pulmonary atherosclerosis, and, therefore, capable of presenting confusing pictures. We shall consider and summarize these pictures and outline the salient points of similarity and differentiation.

Polycythemia, a condition of decided increase in the number of red blood-cells. There are two forms to be distinguished: (1) A relative polycythemia, often termed "erythrocytosis," and (2) an absolute or true polycythemia, or erythremia. The first type is caused by an unusual concentration of the blood, due to copious loss of body fluids, *i. e.*, excessive sweating, or vomiting, or diarrhea. The condition is nearly always transient and is characterized by an inspissation of all the blood elements, by dryness of the skin and mucous membranes, or an anuria, *and by the readiness with which the patient improves after the administration of adequate fluid and salts.* The number of red

blood-cells and the percentage of the hemoglobin rise, but the blood findings and the bone-marrow response of true polycythemia are wanting; moreover, the spleen does not enlarge as in the true type and a tendency for bleeding is unlikely. Cyanosis may be pronounced.

The true, absolute form of polycythemia is called variously, Vaquez-Osler disease, splenomegalic or myelopathic polycythemia, polycythemia with chronic cyanosis, erythrocytosis-megalosplenica (Senator), cryptogenetic polycythemia (R. C. Cabot), polycythemia rubra, or erythremia. These synonyms carry the suspicion that the true pathology is not known or understood. The absolute polycythemia differs from the relative form because it is persistent, chronic (though there may be intervals when the patient is comparatively non-polycythemic, with an apparently normal blood-count, the polycythemic phase reasserting itself before long); it lacks the dry inspissated state, in fact, as a rule, exhibiting congestion of the tissues, even plethora, and it is unrelated to any demonstrable cause for a reduction in the quantity of blood volume. The increase in the total number of *red blood-corpuscles* is remarkable, the figure rising from 6 to over 9 million, and in some cases higher, 12 million (Cabot), 13 million (Koester). This is truly startling in the light of the estimation that a cubic millimeter of blood can hold not much more than about 13 million red cells, but, perhaps, the capacity for storing red blood-corpuscles is altered in erythremic blood.¹ Perhaps, too, the quantity of red blood-cells varies in the larger arterial vessels, in the smaller arteries, in the capillaries, and in the veins; this is likelier if obstruction to the circulation is a factor in the production of the polycythemia. Since we often encounter block of the circulation in pulmonary vessel sclerosis (mitral stenosis), etc., it may be possible to demonstrate here, too, a similar degree of variation in cell count depending upon the source whence blood was

¹ It is claimed that about 13,000,000 red blood-cells is almost the physical limit of "standing room" per cubic millimeter. Osler quotes Mann, to this effect, that there cannot be room for more than 13,900,000 cells per cubic millimeter of blood.

obtained for examination.¹ One should be on guard against error resulting from variations in the technic of the test and in counts which arise from differences in serum content in blood obtained from the subcutaneous tissues or from the vein or the artery, the effect of artificial constriction being important in the two latter instances. Geisbock, in a case of what was probably erythremia, found the same quantity of red cells in the veins and in the arteries.

Correspondingly, the *percentage of hemoglobin* of the blood rises enormously, values up to 160 to 200 per cent. having been reported. The cautions mentioned in connection with the enumeration of red blood-cells obtain here too, perhaps, with greater emphasis, since hemoglobin estimation provides a greater source of error than enumeration of red blood-cells. Generally, the hemoglobin increase does not parallel, to the same extent, the red cell quantitative increase. In most cases there is a color-index below 1; indeed, in some instances there is a very low hemoglobin figure. The color-index is depressed not because there is lack of hemoglobin in each red cell (as is the case in chlorosis), but rather for the reason that the blood circulates an unusual proportion of microcytes; in other words, a large number of red cells are counted as such, but because of their diminutiveness they hold a small amount of coloring-matter.

There is a comparative *leukocytosis* in relative polycythemia, the condition being brought about by the condensation in the blood following upon depletion; but in polycythemia rubra (true, absolute) there is a constant higher level of the total number of leukocytes. Although the figures may not reach those observed in acute infections, leukocytosis is definite, absolute, and, at times, marked (20,000 to 30,000), a dominance of the porportion of polynuclear cells being maintained (80 to 85 per cent. sometimes).²

¹ I can find no reference to an appreciation of this point in the reported cases of pulmonary vessel sclerosis in which cyanosis and polycythemia were present.

² In a discussion of a case of Ayerza's disease, presented by Zeman, Libman raises the question of whether the leukocytosis of erythremia endures through any anerythremic stage. He calls attention also to the lack of knowledge concerning leukocyte counts in Ayerza's syndrome.

In polycythemia, regardless of the type, the *blood viscosity* is increased, reaching figures of 11 to 20 (the viscosity of normal blood is 5.1 to 5.3). Despite this abnormally high viscosity, the blood-pressure need not be elevated, nor is there, frequently, any hypertrophy of the left ventricle. The specific gravity and the percentage of the dry residue of whole blood are increased, while, in the blood serum, they are diminished (their estimation in the blood-serum might prove another item in the differential diagnoses between so-called true polycythemia and other polycythemic states, *i. e.*, that present in pulmonary vessel sclerosis). Parkes Weber maintains that polycythemia rubra with splenomegaly has its origin in an increased activity of the bone-marrow. He believes there is exaggerated red cell formation in the bone-marrow and that this is a primary condition. We may have, then, in true polycythemia (rubra) a primary excessive activity of the red cells in the bone-marrow with the presence of a big spleen associated with cyanosis, displaying a likelihood for hemorrhages in the stomach, intestines, brain, kidneys, pleural and peritoneal cavities, or epistaxis, menorrhagia, and eye symptoms, such as temporary blindness, scintillating scotoma, vertigo. There are no chest pains, but there may be pains in the abdomen. There is no heart enlargement or particular lung engorgement. The general vascular engorgement is not limited to any special organ or structure and may be recognized in any mucous membrane or in the retinal veins. The tongue has a very noticeable bluish-red color. The fingers are not clubbed. The blood changes we have already described in detail. The urine is apt to show urobilin.¹ Though this syndrome picture has its ups and downs, it remains, in the main, lingering, chronic, as a rule, unrelieved, and notwithstanding its suggestive similarity to the polycythemia of pulmonary vessel sclerosis, it is not difficult to recognize it apart, because in the polycythemia with cyanosis of heart or lung disease we have proof of heart or lung impairment. There are, however, polycythemias brought on by other causes which deserve to be recognized and distinguished from true polycythemia or the type

¹ Detailed blood studies for urobilin might prove a profitable field for investigation in the various types of polycythemia.

associated with pulmonary vessel sclerosis. Thus *acute phosphorus poisoning* can lead to a marked polycythemia, albeit very transient (lasting a few days). Likewise, *poisoning from carbon monoxid* can provide a similar picture; here in spite of the marked increase of red blood-cells the hemoglobin may be diminished; *cantharides poisoning* can cause increase of red cells and decrease of hemoglobin in the presence of loss of blood via the kidneys. The *coal-tar products*, like antipyrin, phenacetin, acetanilid, veronal, sulphonal, trional, can alter the blood, causing methemoglobinemia and cyanosis, sometimes bringing on a polycythemia. In these cases there is the history of the poison or drug, the characteristic spectroscopic findings, the absence of chest pain, of bleedings (the urine may be very red, but this need not mean loss of fresh blood), of exacerbations and remissions, the absence of any mechanical factor such as mitral stenosis and no vessel sclerosis elsewhere in the body to invoke the suspicion of pulmonary vessel sclerosis; also there are changes in blood volume and residue, but no leukocytosis.

The *polycythemia of high altitude* can be chronic with a marked increase in the number of red blood-corpuscles and percentage of hemoglobin. The polycythemia encountered occasionally in chronic infection, *i. e.*, syphilis, malaria, tuberculosis, is of remote import here. That a long-standing toxin may produce changes in the blood is not surprising, and that a polycythemic state may represent a blood alteration provoked by toxins acting upon the bone-marrow is not unpalusible. Polycythemia has been described as an accompanying feature of *hemoglobinuria in horses* (McFadyean). Parkes Weber calls attention to the lack of knowledge concerning a probable polycythemia in *Winckel's disease* (cyanosis, jaundice and cherry-red urine, hemoglobinuria¹). Rogers² claims that in Bengal

¹ It would lead us too far afield to enumerate every possible situation possessing any of the symptoms and signs, in varying degree, found in pulmonary vessel sclerosis. Sufficient for the purpose of this paper is the discussion of the more important maladies capable of leading to difficulty in the differential diagnosis. Polycythemia and cyanosis are the outstanding signs of pulmonary vessel sclerosis, and for this reason we have reviewed these essential characteristics of polycythemic conditions.

² Quoted by Warthin in Contributions to Med. and Biol. Res., vol. 2, 1919; also cited in Allbutt's System of Medicine.

there are cases of fatal dropsy with pulmonary arteriosclerosis; he feels the condition is luetic in origin when it affects patients from twenty to forty years of age.

The *duskiness seen in acute infection*, more particularly in myocarditis, pericarditis, in pneumonitis (the cyanosis here may be extreme), should be appreciated as not identical with the intense dark, almost black cyanosis prevailing in pulmonary vessel sclerosis. A moderate degree of cyanosis may appear in coronary disease, a condition to be borne in mind also because of the chest pain—this is unlike the deep-seated “in the lung” variety of pulmonary vessel sclerosis, rather typical in spread and limitation, and likely to be associated with a clutching vise-like sensation about the heart and a terror of impending death. There may be overwhelming physical weakness and prostration. The milder seizures can present milder symptoms. In coronary attacks we search for a history of previous paroxysms, for evidences of sclerosis elsewhere in the body, *i. e.*, intermittent claudication, narrowing of the blood-vessels with diminished pulsation in the extremities. The blood-pressure is often low during the attack (though occasionally it may be higher during a paroxysm); a temporary leukocytosis frequently appears at the time of an acute attack, and there may be definite, though fast disappearing signs of pulmonary edema, more especially at the bases. We do not expect hemoptysis.

That **myocarditis** alone, with or without arrhythmia or chronic valvular disease, can bring on lung engorgement is well known. Of the specialized condition for lung engorgement, due in some way to mitral stenosis, we have already spoken. But valvular damage anywhere in the heart may lead to lung vessel engorgement with usual signs of heart decompensation, edema of the tissues, accumulations of fluid in the cavities, and intensification of symptoms upon exertion. We must separate the diagnosis of heart affection with cyanosis, cardiac pain, and the likelihood for hemoptysis from pulmonary vessel sclerosis by a history of heart infection, the absence of attacks of long-standing bronchitis, and the absence of prolonged progressive cyanosis or polycythemia.

Pericarditis, in its acute form, may have a constricting jacket of fluid exert pressure upon the vena cavæ, fluid accumulating under the sulci which run between the great vessels and the auricles; cyanosis may be intense and of short duration. There is no erythremia, there is no deep pain, hemoptyses are not unexpected. In the adhesive type there will be the local signs characteristic of the condition, *i. e.*, lack of mobility of the heart upon change of posture, *x-ray* evidence, also the local retraction in systole, and symptoms due to deranged cardiovascular mechanics, *i. e.*, engorged veins, pulsus paradoxicus, anasarca, enlarged liver (often perisplenitis). There can be cardiac pain and fever.

An intense cyanosis may be traced to an *abnormal intercommunication of arterial and venous blood*. This is obviously true of congenital hearts, but I have in mind now the communications found in arteriovenous anastomosis often aneurysmal in nature; thus, if any aneurysm exert pressure upon the thoracic veins there will be evidence of compression; if perforation takes place the cyanosis can be extreme, and with pain, hemoptysis and signs of heart embarrassment can ensue. How misleading and perplexing the diagnosis of such a case may be is illustrated by the following history of aortic aneurysm which almost succeeded in establishing an artificial communication between itself and the pulmonary artery. The conspicuous absence of cyanosis and polycythemia were difficult to reconcile with a clinical diagnosis of luetic pulmonary arteritis or pulmonary vessel sclerosis or artificially produced anastomosis between pulmonary artery and aorta. The autopsy findings explained why the local heart signs, suggestive as they were, failed to support fully any of these diagnoses.

G. Mc., a man fifty years of age, a painter by occupation, was admitted to Dr. Mosenthal's service at the Post-Graduate Hospital (Case No. 46,228) on October 8, 1924.¹ The patient said that he had had chancre,

¹ This case is reported through Dr. Mosenthal's kindness; I wish also to acknowledge my appreciation of his help and co-operation. To Dr. Klemperer I owe the autopsy protocols of the cases from the Post-Graduate Hospital and I am indebted to him for continuous and generous counsel.

also gonorrhea, twenty-five or twenty-seven years ago; about twenty years later he had experienced abdominal cramps (probably tabetic crises). For six months prior to his admission he was aware of dyspnea, orthopnea, heart palpitation and headache, and blurred vision. Within the last month he suffered an attack of loss of consciousness and he developed noticeable aphonia.

The physical examination disclosed a patient of muddy ashen complexion very slightly cyanotic, but extremely short of breath. He had visible large pulsations in the suprasternal notch and in the neck, and a suggestive Corrigan pulse. There was no pulsus paradoxicus or any anacrotic or bisferien quality in the pulse. A pistol shot sound was heard in the carotid vessels; the blood-pressure was 115/40. The chest had a widened zone of retromanubrial dullness as for a widened aorta. There was no left ventricle "choc en dome." Over the pulmonic (Balfour) area there was a long continuous systolic rumble, soft, filling almost the entire heart time cycle, transmitted into the apex and also across the midsternal line. A soft systolic bruit from the tricuspid area propagated itself downward toward an enlarged, tender, pulsating liver. The spleen was not felt. The abdomen and the thorax cavities had free fluid, and the limbs were moderately edematous.

The patient's illness in the ward was afebrile without leukocytosis; gradually progressive heart failure signs developed. One day before his death the clinical note reads "cardiac failure in a patient with myocardial disease plus aortic enlargement and dilatation (luetic aortitis), also narrowing of the isthmus, relatively. The right coronary artery may be involved. The absence of cyanosis makes it difficult to consider luetic pulmonary artery disease *per se*."

The laboratory reported a strongly positive Wassermann blood test, but a negative spinal fluid Wassermann and colloidal gold reaction. The blood count was 5,016,000 red blood-cells and 7680 white cells. The non-protein nitrogen figure was 45 and the urea nitrogen was 19.2. Upon x-ray the heart was made out to have all its chambers enlarged and there was an enlargement of the pulmonic and left auricular areas.

October 23, 1924 the patient died, and his autopsy revealed a luetic mesortitis of the ascending arch and descending portions. (Dr. Klemperer was able to demonstrate spirochetæ in the aorta.) There were three aneurysmal bulges of the ascending aorta and arch, one of which had almost succeeded in boring through into the pulmonary artery, truncus arteriosus. There was insufficiency of the pulmonary and of the aortic valves and an eccentric hypertrophy of both ventricles. The body showed ascites, hydrothorax and anasarca, hyperemia of the spleen, the kidneys and the liver (with fatty infiltration).

Congenital Heart Disease.—Not all cases have symptoms or signs; on the other hand, the diagnosis often is plain from birth, as in morbus cœruleus (due to pulmonary stenosis as a rule); the congenital malformation may be of the septa or exist at or

in the valves, or there may be a marked narrowing at the aortic isthmus or in the pulmonary orifice. Failure of closure between the aorta and pulmonary artery (open ductus botalli) is a frequent lesion. A recognition or differentiation before autopsy of the congenital defect may be futile. The diagnosis, nonetheless, may be established often by a history of unrelieved cyanosis, by the polycythemia unaccompanied by an enlarged spleen unless there is chronic passive congestion, by the dyspnea, and by the clubbing of the fingers and toes. In some instances the dyspnea is apparent upon exertion only and the cyanosis wanes or deepens in wave-like periods of remission. If there be a persistent fetal aortic stenosis, we may be able to observe a striking difference in the sizes of the arteries of the upper and lower halves of the body, those in the lower half being smaller, narrower, and the pulsation smaller and delayed as compared with the larger pulse in the larger arteries of the upper half of the body. In any form of congenital heart defect we may find signs of impeded circulation as the heart begins to decompensate. There is also a form of mitral stenosis probably congenital, described by Duroziez.¹ In any type of congenital heart disease the stature of the patient may be small, well below the required

¹ Intra-uterine infection, luetic or rheumatic fetal endocarditis, is not eliminated as a responsible cause, nor is a congenital anatomic defect established as the undisputed explanation for this condition. Nevertheless, it would appear that congenital mitral stenosis probably exists. We cannot say, for certain, that an acquired infection, very early in infancy or babyhood could not have produced the lesion, but whether intra-uterine or acquired, its influence upon the lesser circulation could be profound, the effect becoming manifest before birth, if congenital, or very soon after birth if acquired; in either event a so-called "pure mitral stenosis" could enter into the causation of pulmonary vessel sclerosis.

Duroziez (*Arch. Generales*, ii, 1877) is quoted by M. H. Bass (*Arch. of Ped.*, February, 1916), with the following description: "Pure mitral stenosis, *i. e.*, without a murmur of insufficiency, without much dilatation of the auricle, without lesion in the lung, is more frequent than was believed. It is easily overlooked, the patients being troubled very little and having in no way the appearance of cardiacs. The heart is normal in size and impulse. The pulse is regular. Pallor is remarkable. The first sound is strikingly loud. The onset is often difficult to fix and may go back to infancy. Often one fails to find the history of any acute disease. It is commoner in women. It is compatible with long life."

standard of the patient's corresponding age. Over the heart we should find signs of enlargement of the ventricles or characteristic enlargement of the pulmonary artery and conus, but such evidence (enlargement, thrill, murmur) may not be discernible. A stenosed tricuspid valve can produce a picture of intense cyanosis.

In contradistinction to pulmonary vessel sclerosis in congenital cardiacs we can have an intense cyanosis from birth, rarely assuming the deep, almost black character observed in pulmonary vessel sclerosis; there is clubbing of the fingers and toes, but no deep lung pain. There are physical signs over the heart and in the vessels of the mechanical defect, there is little tendency to bleedings from the lungs; these patients are of underdeveloped stature, frail, vulnerable to intercurrent infection, and seldom live with advanced lesions beyond the third decade of life. A marked degree of cyanosis can go with a transposition of the great vessels of the heart either with or without partial or complete situs transversus. The cyanosis and the polycythemia, if present, date from birth, and are not developed in people who have been hitherto healthy, as is the case in pulmonary vessel sclerosis. Clubbing of the fingers may or may not take place.

Ayerza's Disease.—This disease, clinically described by Ayerza of Buenos Ayres in 1901, represents, according to him, a leucic process of the pulmonary artery and its branches leading to atheroma and sclerosis of the pulmonary radicles. In addition to Ayerza, his pupils and other South American observers, similar conditions have been described by Parkes Weber, by Warthin, who was the first to report such a case in this country, and by Zeeman. Clinically these patients tell a story of recurrent respiratory troubles, asthma, bronchitis, with dyspnea either provoked upon exertion or spontaneous and constant, accompanied also by cyanosis. The cyanosis develops until the dark, black-like color results. Indeed, the South Americans term these cases black cardiacs (*cardiacos negros*). The cyanosis goes hand in hand with a secondary polycythemia. Several observers claim that the polycythemia or erythremia is a sec-

ondary compensatory process, indicating greater activity of the bone-marrow to overcome the lack of oxygen following upon the obstruction in the pulmonary circulation due to sclerosis of these vessels. There is, therefore, no true polycythemia here, and in this knowledge an enlarged spleen, when found, is to be regarded as another secondary feature, brought about, late or early, by chronic congestion or by an increased demand for spleen function and not as an integral part of the polycythemic picture. The erythremia is marked, 6 to 10 million red cells; the white cell count is not increased (Warthin's case, Zeeman's case); the bone-marrow (in Warthin's case and in Parkes Weber's case; there is no description on this point in Zeeman's case) showed definite erythroblastic hyperplasia. Ayerza's disease is not essentially related to the heart. We have no mitral stenosis as part of the picture, but eventually the steady march of sclerotic development in the lung vessels with its ensuing and ever-increasing demand upon the right side of the heart produces an almost overwhelming hypertrophy of the right heart. In fact, at this time the x-ray picture may delineate a large right ventricle with its right outline extending well out to the right of the sternum. Of special clinical interest and value is the luetic basis for this disease (an opinion in which Parkes Weber does not concur, he maintaining that syphilis is a coincidental discovery, but Warthin's careful microscopic study of the pulmonary artery revealed latent syphilis; Zeeman's case was also luetic). There is a slow-moving, but prolonged picture of lung trouble, asthma, bronchitis or dyspnea, recurrent in nature, and gradually overtaken by a slow, on-creeping cyanosis lasting over a period of years deepening until an almost purplish bluish (black) color is reached. Polycythemia is present and persistent, secondary upon a bone-marrow derangement, showing no leukocytosis and rarely any abnormal red cells. Dyspnea is a variable symptom; there may be enlargement of the spleen, the fingers may or may not be clubbed, and finally secondary symptoms are discovered, following upon the enlargement of the right side of the heart, the wall of the right ventricle attaining, perhaps, the thickness of that of the left. Pain is not usual,

but an additional point of clinical interest in the differential diagnosis is the eye picture found here as well as in true polycythemia, a point emphasized by Parkes Weber, *i. e.*, extreme distention of the veins of the retina with very tiny blood-vessels, some of the veins having a slight moniliiform appearance.

Respiratory Conditions.—Cyanosis, dyspnea, pain in the chest, hemorrhages from the lungs are observed often in affections of the respiratory system. Any mechanical obstruction, acquired or congenital, in this system can produce cyanosis, dyspnea. The diagnosis, however, should offer little difficulty in its differentiation from pulmonary vessel sclerosis.

Emphysema, alone or with bronchitis or some clinical type of asthma, may lead to pronounced cyanosis. This we have seen in case 3567-A, probably. The exaggerated distention of the air sacs in the lungs produces hypertrophy of the right side of the heart and resultant cardiac derangement; the process in the lungs eventually obliterates the lung capillaries and so impedes the flow in the lesser circulation. Marked emphysema by itself, therefore, may produce a picture resembling in large measure that of pulmonary vessel sclerosis. More often emphysema is responsible for and associated with sclerosis of the pulmonary vessels. If infection exists in the lung, particularly bronchiectasis, clubbing of the toes and fingers is likely. Patients with emphysema usually have repeated seizures of dyspnea ("cardiac asthma"), cough, expectoration, sometimes profuse, cyanosis, even of a very severe grade, together with hemoptysis, and finally signs of heart failure. The diagnosis is not difficult, since these patients are of middle or advanced years and have a history of respiratory infection, a rather typical chest contour with definite physical lung signs of emphysema. A protracted existence of emphysema should arouse the idea that the pulmonary vessels may be undergoing atherosclerosis at the same time.

Tuberculosis.—The chronic fibroid type or the miliary form in the lungs or general miliary tuberculosis may produce hemoptyses, dyspnea, cough, and, in some patients, cyanosis. Frequently there is a superadded secondary infection. Tubercular

patients are prone to show fever, wasting, constitutional symptoms of a reaction to a toxic substance, tubercle bacilli in the sputum, and clubbing of the fingers if there be a secondary lung infection. Cyanosis is almost never extreme and polycythemia is absent. Instead there is anemia, malnutrition, and no preponderance of the right heart.

Abscess, gangrene, foreign body, actinomycosis, cyst in the lungs, unresolved pneumonia or interstitial pneumonitis (lues, chalicosis—stone dust, siderosis—iron dust, anthracosis) may bring about confusing pictures.

Embolism, Thrombosis, and Infarction.—The pulmonary artery or its branches may be blocked by an embolus or thrombus; this occurs in chronic heart disease or in general infections, as typhoid, and upon the nature of the embolus will depend the clinical result of the infarction, *i. e.*, absorption or abscess, or pneumonitis. Symptomatically, there may be fever, chill, blood-tinged sputum, dyspnea, cyanosis, and leukocytosis. During the acute process there should be no confusion in its recognition from pulmonary vessel sclerosis. Not infrequently infarcts in the lung may be symptomless and undiscovered.

Bronchial Asthma.—This is a condition of paroxysmal seizures, of shortness of breath, cyanosis, pain in the chest, with signs in the chest of loud sonorous râles. The sputum has Curschmann spirals, Charcot-Leyden crystals, and many eosinophils, also the blood has an eosinophilia, sometimes very pronounced. Related to these paroxysms clinically, but differing probably basically, are the similar attacks of asthma, dyspnea, cyanosis, etc., induced by pollinosis, or by anaphylactic reaction to food proteins, to animal emanations, to dust, to talcs, and, perhaps, to bacteria. Cardiorenal diseases, too, are supposedly responsible for asthma. But whatever the cause, asthma, unlike pulmonary vessel sclerosis, clinically exhibits no polycythemia, no hemoptysis, as a rule, and no story of cyanosis, dark purplish in hue, slowly progressing over years.

Pneumothorax.—The acute form may be announced by sudden sharp pain in the chest, severe cyanosis, and dyspnea, with a general picture of collapse. Not seldom a pneumothorax,

though extensive, develops insidiously and remains undetected. Usually the clinical picture is unmistakable, especially when considered in the knowledge of an antecedent history of pulmonary tuberculosis or lung infection of any character, emphysema, abscess, gangrene, or when a sudden exertion or thoracic trauma abruptly produces these startling symptoms. The condition is usually unilateral, although bilateral involvement is known. Under certain circumstances, *i. e.*, pleural adhesions, lung consolidations, or fluid sacculation, the pneumothorax can be limited and small. Barlow and Thompson have written an able monograph on the subject of partial, small, circumscribed pneumothoraces. When a pneumothorax collapses sufficient lung over a long period of time, there will be intense cyanosis approaching the gray, muddy, almost black color conspicuous in pulmonary vessel sclerosis or in Ayerza's disease. The diagnosis, however, is comparatively easy through the aid of the x-ray plate and fluoroscopic screen. In addition, there are, over the implicated area, chest immobility, absent breath sounds, exaggerated percussion resonance, displacement of heart, liver, diaphragm. Furthermore, polycythemia is not evident, nor hemoptyses, nor pain within the lungs. The criteria enumerated for the differential diagnosis hold in the clinical separation of pulmonary vessel sclerosis, not only from pneumothorax but also from atelectasis, subphrenic conditions such as pyopneumothorax, cyst, diaphragmatic hernia, or eventration of the diaphragm or the peculiar condition of collapse of the lung, or an unusually large tuberculous lung cavity.

Acute gastric dilatation and *acute pancreatitis* may produce an unexpected and distinct cyanosis. These are acute conditions and the cyanosis is of short duration.

Mediastinal Diseases.—Respiratory and cardiac embarrassment can be pronounced in pathologic situations affecting the walls of the mediastinal spaces or their contents. Alterations, inflammatory or neoplastic, of the trachea, esophagus, aorta, or lymph-nodes sometimes cause dyspnea, cyanosis, engorgement of the veins of the head, neck, arms, chest (but not of the legs), aphonia, cough, and substernal pain. A hypertrophied or

tumor-bearing thymus gland, a substernal goiter, a new growth of the lungs, pleura, or hilus glands, or a dermoid cyst may be the responsible agent for a clinical picture resembling pulmonary vessel sclerosis, but in mediastinal diseases we have a cachexia in malignant neoplasm (though primary malignant lung neoplasm may run a very slow almost cachexia-free course), no polycythemia, and there may be clubbing of the fingers in inflammatory and suppurative conditions. Further information in the differentiation is obtained from the blood examination, from the presence of new growth, or lymphatic involvement elsewhere in the body.

Purpuras.—Repeated hemoptyses may be observed in purpuric diseases. A study, therefore, of the blood, its platelets, coagulation and bleeding time, clot retraction, fragility of the red cells as well as the total white, red blood-cell count and hemoglobin estimation, together with the history, will generally establish a diagnosis of purpura. Splenomegaly is found with many blood diseases and many blood diseases have a tendency to cause petechiæ or larger hemorrhagic areas or frank loss of blood through the mucous membrane (a striking illustration is to be noted in so-called thrombocytopenia, described and discussed by Kaznelson and by Brill and Rosenthal and others).¹

Ochronosis.—This is a very rare metabolic disturbance, usually congenital and probably hereditary (when it does occur it is observed in several members of one family). The malady lasts through life and is characterized by a bluish, black coloration of the cartilages and of the skin and scleræ. The deep pigmentation may simulate a chronic, severe cyanosis. The diagnosis is made by the lesions of the joints and cartilages and by the presence of alkapton in the urine.

SUMMARY

A detailed critique must await our completed pathologic investigation. At this time, however, we can point to the differ-

¹ Griffin, H. Z., and Holloway, J. K., in the *Amer. Jour. Med. Sci.*, August, 1925, p. 186, review 28 cases of purpura hæmorrhagica in which splenectomy was performed. The article discusses the clinical aspects of this condition and contains bibliography references up to date.

ence in pathologic picture between the so-called primary and secondary types of pulmonary atherosclerosis. In the former the lungs' finer radicles suffer, the larger vessels escaping practically intact, while in the secondary type the brunt of the impairment is borne by the medium and larger sized blood-vessels. In the text a comparison of cases H. L. and A. P. H. illustrates this difference, even though H. L. was not entirely free of an associated disorder inasmuch as he had a marked emphysema.

A survey of our autopsy material emphasizes the significant rôle which mitral stenosis bears in the genesis of hypertension of the lesser circulation and eventual vessel sclerosis alteration. The four tables printed demonstrate that mitral stenosis was found thirty-seven times at autopsy in patients who had no atherosclerosis of the greater or lesser systems. On the other hand, in 18 cases of pulmonary vessel sclerosis and no general sclerosis, the mitral valve was markedly constricted in fifteen instances; only nine times was it stenosed in patients who had atherosclerosis of the general and lung arterial systems, but out of 80 cases, where there was marked general arteriosclerosis, but no pulmonary sclerosis, the mitral valve was stenosed in one instance only.

Clinically, we are concerned with a slow moving, but ever-deepening cyanosis until the skin assumes almost a plum color. This intense, impressive cyanosis is strikingly disproportionate to a mild or even absent dyspnea. A high grade of polycythemia is not unlikely, but its nature differs in some important respects from true or absolute polycythemia. Pain is by no means constant. Its appearance may be paroxysmal (Posselt describes this as "dyspragia intermittens, angiosclerotica, pulmonis"), its character is ill-defined, vaguely described as "deep within the lungs," but quite unmistakably unlike the typical angina anguish of coronary seizures. Hemoptysis also may be recurrent or entirely absent. In fact, an antecedent history of exacerbations and remissions of chest pain, lung bleeding, aggravated by cyanosis, asthma, etc., is not uncommon. Clubbing of the fingers and toes is unusual, indeed, some authors claim it does not occur. There is no body wasting, no cachexia,

no leukocytosis. The course of the condition is likely to be afebrile. When cardiac compensation breaks, edema, etc., may appear. The x-ray and fluoroscopic examinations yield helpful data, *i. e.*, enlarged right heart, relatively small left heart, or enlargement of the conus, absence of pulmonary stasis, as found in cases of mitral stenosis. In general, the syndrome is fairly well defined, and its presence should suggest the possibility of sclerotic involvement of the lungs' blood-vessels; in the absence of heart or lung disorders this clinical picture may represent a so-called primary pulmonary vessel sclerosis. The diagnosis of either form of lung vessel sclerosis, however, may be hazardous and difficult to separate, as indicated in the text, from a number of conditions with simulating pictures. We are not prepared to say, now, whether clinically one may distinguish clearly between primary and secondary sclerosis.

Finally, the bearing of infections upon the entire problem of pulmonary blood-vessel involvement has a particular interest for the clinician. Here belongs the consideration of such specific infections as syphilis, gonorrhea, variola, or the possible relationship of sclerosis of the pulmonary artery and its branches to clinical entities like Ayerza's disease, Raynaud's disease, or thrombo-angiitis obliterans (Buerger).

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SYPHILIS OF THE STOMACH*

THE subject of gastric syphilis is very interesting because of its curious and variable symptomatology, difficult diagnosis, and treatment. Although it was formerly considered extremely rare, it has now come to be more easily recognized by our modern methods, and has been found less infrequent than was supposed. In every case of unusual gastric symptomatology or roentgenologic findings its presence must be considered.

True gastric syphilis implies a definite syphilitic lesion, such as a tertiary lesion, especially a secondary mutilating sclerosis, gumma, or gummatous ulcer.

The first case of syphilitic gastritis was reported, says Cronin,¹ by Andral,² who claims to have cured 2 cases by treatment with mercury. Our knowledge of gastric syphilis before 1905 was obtained chiefly from postmortem material. From then on to 1910 the response to antisyphilitic treatment was a great aid to diagnosis. During the last decade this subject has been developed by Smithies, Morgan, Meyers, LeWald, Downey, Einhorn, Eusterman,³ Carman, and others.

Syphilis of the stomach is a rare disease occurring probably less than 1 to 100 other organic lesions of the stomach, such as ulcer and cancer. It occurs in early middle life and averages twice as frequently in men as in women. It usually occurs in the fourth decade, while cancer generally comes later. The duration of symptoms is shorter than in ulcer and longer than in carcinoma. The symptoms occur on an average of twenty years after the primary lesion and they usually last two years.

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PATHOLOGY

The pathology is a terminal mutilating sclerosis resulting in contractures involving the gastric walls with a tendency to hour-glass or annular prepyloric contracture.

Broad local contractures are characteristic, as also are smaller infiltrations, which result in diminished capacity of the stomach. Occasionally there have been reported stomachs like a stiff-walled tube, holding but a few ounces. These are usually congenital cases.

This diminished capacity of the stomach frequently leads to insufficiency and consequent incompetency of the cardia and the pylorus. The extent of the lesion is actually greater than one would imagine by seeing the roentgenogram.

We may divide gastric syphilis into two clinical forms: The first is the obliterative annular pyloric contracture, and the second, the bilaterally contracted hour-glass terminal sclerosis which is not always characteristic of syphilis. The histologic picture is not amenable to antisyphilitic treatment like most other syphilitic scarring.

Such scleroses are the result of exudates, gummata, or gummatous ulcers. The lesions may represent any composite of various phases. The process may be erosive, ulcerative, exudative, or gummatous; or it may be varying degrees of the above. Thus the pathology gives rise to the variable symptoms of ulcer, gastritis, carcinoma, and pyloric stenosis. There is no proof as to secondary lesions occurring in the stomach. The syphilitic ulcer is commonly multiple. It covers considerable area, is shallow, and has a heavily infiltrated base.

Syphilitic ulcers are serpiginous, sharply defined, have somewhat raised edges, and are frequently hemorrhagic. The base is so infiltrated at times as to resemble carcinoma, especially when this infiltration occurs at the pyloric end of the stomach. Occasionally there is a perigastritis. Perforations rarely occur.

The lesion usually consists of dense connective-tissue infiltrations with collection of perivascular lymphoid cells. There are also collections of cells of epithelial type in the connective tissue. Multinuclear giant-cells may be present. The final

proof of a syphilitic infiltration would be the identification of spirochetes in the affected tissue, but this is not usually accomplished.

SYMPTOMATOLOGY

There is a lack of any characteristic symptoms. Pain is not prominent, but is present in 50 per cent. of the cases. The pain is not like that of ulcer, but is less subject to relief by alkalies. In sclerotic cases pain occurs on eating, like that in non-obstructive gastric carcinoma, and is relieved by vomiting. Nausea is infrequent. Vomiting and flatulence are common. There is occasionally regurgitation from the cardia into the lower esophagus. The appetite is generally good and occasionally may be ravenous.

There are occasional symptoms simulating gastric ulcer, in the prepyloric obstructive type, which are sometimes interpreted as gastric crises by the clinician. There is great loss of weight which occurs more gradually than that occurring in patients with carcinoma. When symptoms first occur in gastric syphilis there are extensive lesions seen by x-ray which is certainly not the case in gastric carcinoma. These early gastric symptoms in syphilis are transitory. In carcinoma the symptoms are progressive.

DIAGNOSIS

The physical signs are anemia, cachexia, emaciation, and other objective evidences of syphilis. A palpable mass is rarely present.

The blood Wassermann reaction is positive in a large proportion of the cases, although occasionally a provocative dose of arsphenamin is necessary. There may be achylia, a subacidity, or an acidity of the gastric contents. Occult blood in the stools is found less frequently than in the stools of patients with carcinoma.

LeWald⁴ classifies the Roentgen findings as follows:

"1. Diminished size of stomach accompanied by an almost insured evacuation of its contents. Traces of food, however, may remain at cardiac end for six hours or longer.

"2. Dumbbell-shaped deformity due to stenosis of the middle of the stomach over a wide area in contradistinction to the hour-glass stomach from a cicatrized ulcer involving a circumscribed area. In this type there is apt to be a compensatory dilatation of the esophagus to offset the diminished stomach capacity.

"3. The infiltration may involve only the pyloric region, in which case the findings may closely resemble those of a cicatrized ulcer in the same region and may be accompanied by dilatation of the stomach.

"4. Filling defects about the greater curvature or any portion of the stomach, in which case the findings may closely resemble new growths."

The diagnosis is aided by the contrast of a large gastric defect which is out of all proportion to the comparative good condition of a patient. The patient is usually too young for cancer and gives a longer history. The history is like that of ulcer, but food and alkalis do not relieve pain. There is an absence or marked reduction of the gastric secretion. There is the lack of palpable mass where such would be expected. There are positive serologic reactions. A history of syphilis is usually given. There is concomitant evidence of a syphilitic infection. The Roentgen findings are positive. The therapeutic evidence is the relief by antispecific therapy, but this is not necessarily true. The most important diagnostic point is the surprisingly extensive lesion by x-ray without a palpable mass in patients too young for malignancy, not ill, and giving an unduly long uncharacteristic history with a positive Wassermann reaction.

PROGNOSIS

The prognosis varies with stage of the lesion and the amount of the sclerosis. It is good in the gummatous and gummatous ulcer stages. The symptoms disappear and the roentgenographic picture of the stomach improves, though the defect does not entirely disappear.

Even in sclerosed cases the patient may be helped by raising the general resistance and by controlling the syphilitic

condition. Surgery is helpful in hour-glass, prepyloric contraction, and other deforming changes interfering with motility. The worst cases are those with thickened gastric walls and lessened gastric capacity, with incompetent pylorus and cardia, and dilatation of the proximal small intestine. In these cases an impaired digestion occurs in the small intestine.

TREATMENT

Antisymphilitic treatment should be given in all suspected cases. An exploratory laparotomy and examination of tissue may be done if necessary. Treatment should be continued persistently even though there is no relief in symptoms, as lesions amenable to treatment may be present along with scars.

Where the motility is seriously affected and there is no change with therapy, gastro-enterostomy may be done. Resection is advisable for marked hour-glass or prepyloric contractures. Other medical treatment consists of placing the patient on a soft ulcer diet. He should have frequent small meals. Dilute hydrochloric acid may be sipped with his meals. He may have iron as a tonic, preferably by hypodermic injection. Lavage performed carefully also gives relief.

The following case has come under my observation:

A young Jewish clerk of nineteen came to me in January, 1922 complaining of upper abdominal distress and vomiting. His family and previous history were essentially negative, although he recalled a similar attack of gastric disturbance seven years previous. There was no history of venereal disease. His symptoms had persisted for the past year and have been aggravated during the past three weeks. There was no pain, but a sensation of epigastric fulness, occurring from a few minutes to two hours after eating. This condition was relieved by the vomiting of ingested food. There was a moderate amount of belching with tasteless eructations. Constipation was present. There had been a slight loss of weight. There was gradual increasing weakness.

The physical examination showed normal corneal reflexes. The patellar reflexes were moderately exaggerated. There

was marked dental caries. The abdomen was of the scaphoid type and there was a slight tenderness in the supra-umbilical region. The sigmoid was filled and spastic. The patient's weight with his clothes on was 94 pounds.

His fasting gastric contents at that time amounted to 25 c.c. and contained no free hydrochloric acid. An examination of this aspirated material was essentially negative microscopically. After the Ewald test-meal 150 c.c. of gastric contents were

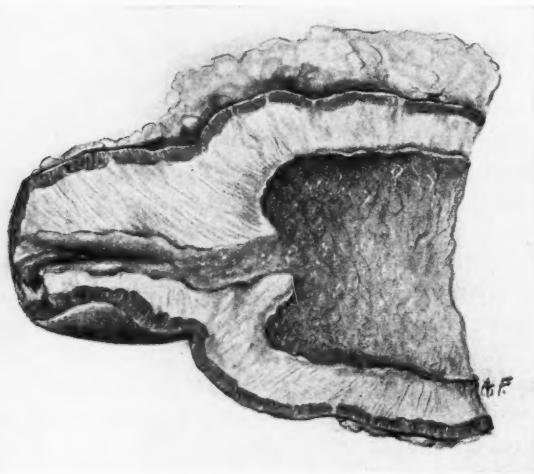


Fig. 120.—Thickened pyloric wall showing almost complete stenosis.

obtained and the titration showed a total acidity of 10 and again an absence of free hydrochloric acid.

Fluoroscopy showed a normally placed stomach with hyperperistalsis, but no emptying through the pylorus. There was an apparent insufficiency of the cardia with regurgitation back into the esophagus. There was no tenderness over the pylorus. The lower esophagus was dilated. One-half hour later, the patient having vomited in the meantime, there was still a large amount of retention in the stomach. Six hours after the contrast meal there was still marked gastric retention, practically

no food having passed through the pylorus. Since there was practically complete pyloric obstruction and the patient was rapidly going down hill, operation was deemed advisable. A colloid-like tumor, found occupying the pyloric end of the stomach, was resected and a gastro-enterostomy done. The pyloric wall was tremendously thickened and there was an almost complete stenosis (Fig. 120).

The resected portion showed diffuse inflammatory infiltration, especially marked in the submucosa and mucosa, with super-



Fig. 121.—Mucous membrane at site of defect, showing marked round-cell infiltration with the destruction of glands and replacement by granular tissue.

ficial necrosis. The mucous membrane at the site of the defect (Fig. 121) showed marked round-cell infiltration with destruction of the glands and replacement by granular tissue. The submucosa (Fig. 122) was very much thickened and showed fibrosis and thickening of the arterioles with many areas of perivascular infiltration by plasma-cells. There was also some round-cell infiltration of the muscularis and subserous capil-

laries and the capillaries in the musculature. This lesion would correspond to a syphilitic inflammatory process involving the stomach wall.

There was an uneventful convalescence until February 9th, when the patient suddenly took a turn for the worse. His breathing became labored and his pulse imperceptible. He died on the following day. Necropsy showed syphilis of the stomach, myo-

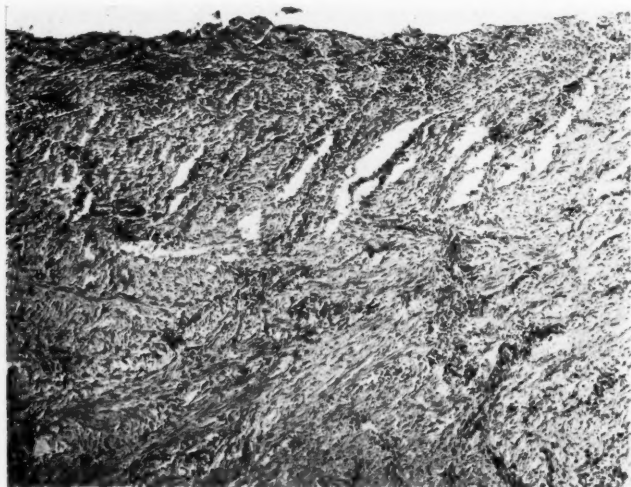


Fig. 122.—The submucosa very much thickened, showing fibrosis and thickening of the arterioles with many areas of perivascular infiltration by plasma cells and round-cells.

cardium, liver, and kidneys. There was a focal arteriolar nephrosclerosis, an acute peritonitis, and purulent infarcts in the lungs.

I wish to thank Dr. F. S. Mandelbaum for the courtesy of allowing me the use of the pathologic material in this case.

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THE INFLUENCE OF FOCAL INFECTION IN THE NOSE, THROAT, ACCESSORY NASAL SINUSES AND TEETH, AND THE SIMULTANEOUS ANOXEMIA ON INTERNAL MEDICINE. SOME ILLUSTRATIVE CASES

THAT the nasal fossæ structures and those immediately surrounding it (paranasal sinuses), the pharyngeal structures and dental organs, are more and more coming to be regarded as the principal bodily organs that give rise to focal infection and absorption is daily becoming more evident to the profession as a whole.

It is of the greatest importance to understand just how abnormal states of the nose and throat injure the body, and the exact manner in which this evil work is done. These abnormalities cause injury directly in two ways: (1) A distorted, swollen state of the nose and throat interfere with proper oxygen supply to the body, due to the fact that air cannot properly be prepared by abnormal noses for absorption in sufficient quantities by the lung tissue. This brings about the state of suboxygenation which, in other words, is a deficient supply of oxygen to all the tissues and organs. It is expressed by such terms as lowered resistance, run-down condition, lowered vitality, anemia, etc. (2) This method is equally direct. It is germ or toxin absorption from the various accessory nasal sinuses, the teeth, the nasal fossæ structures, any component of Waldeyer's ring, such as the adenoid structures or their remains, the faucial tonsils, pharyngeal lymphoid tissue, or the lingual tonsils. In the case of younger people (as a rule) we have the sinuses, tonsils, adenoids, or the nasal fossæ structures themselves, mostly to deal

with. In older people and the old we have the sinuses, the nasal fossæ tissues, the teeth, and frequently the tonsillar tissues. Absorption from the sinuses or teeth is very similar to absorption from diseased, swollen, or non-swollen tonsils. In the young the diseased tonsils and adenoids are frequently, but far from always, the chief factor. Whereas, in the older, absorption from the nasal fossæ structures, sinuses, and teeth is often the principal factor. There is a decided similarity between the *modus operandi* of the two. It is undoubtedly a fact that disease of these upper structures gives rise to badly infected teeth. This later factor then becomes one of their strongest allies in causing harm and damage to distant organs. It is undoubtedly a fact that sinusitis in itself (with the aid of suboxygenation-mouth-breathing) causes this condition. In the infant and very young we can practically eliminate the factor of focal absorption from teeth, since they have no teeth or very few teeth. This is also a very convincing reason for regarding the origin of focal infection in the nose and throat and not in the dental structures, and inductive logic compels us immediately to look for these conditions, and infection in the nose and throat structures or sinuses, in every case that presents itself with poor teeth.

Of all misnomers, the term "focal infection" is the greatest. The idea expressed is not sufficiently comprehensive; it is really more than focal infection. The plain word, poisoning (of the body), would possibly be more expressive and truthful. And this does not go far enough. That it is an interlocking affair between what we can consider simultaneous poisoning and interference with the oxygenation of the body is self-evident to the student. If regarded in this light it is logical, simple, easily understandable, and correct.

Hence, not for a moment is it to be forgotten that the chief and essential ally of focal infection is anoxemia. And that the remarkable thing about it all is the fact that these two allies are simultaneous in their origin, growth, and course.

Suboxygenation (anoxemia) gives rise to suboxidation. This is undoubtedly the explanation for the state of lowered resistance so commonly found in people nowadays. If the body cannot

seize sufficient oxygen, naturally all the bodily functions will not be properly performed. Assimilation, digestion, nutrition, elimination are all dependent on a proper amount of oxygen for the correct chemical combinations and formation of new compounds that occur in the various bodily processes. The chemistry of the formation of all these compounds is interfered with. We call the end-result lowered resistance, lowered vitality, run-down condition, etc. But in its final analysis it means just one thing—interference with the body chemistry.

It is a question whether all focal infection is not primarily a bacterial incubation process of one or more of the nose and throat structures. It invariably has its source of origin in the nose and throat, and the harm done is always direct; there is nothing mysterious about it. It is a simple process of poisoning. If we take in so much poison, we get so much injury.

Some people are more susceptible to these infections than others. This is principally explained by anatomic formations of the nose and throat and poor bodily resistance. And again, poor bodily resistance is explained and dependent on anatomic formations. That is, were the anatomic formation perfect, the bodily resistance would be perfect. The term "poor bodily resistance" is inaccurate, more in the sense of an excuse; and what really counts is the anatomic distortion of the nose and throat. This practically explains the origin of the vast majority of ills to be found in human beings. A check-system, which the writer has developed, assists decidedly in arriving at this conclusion. This method consists of a simple antisepticing treatment of the entire nose and throat area, from which we can invariably expect certain local or distant results when administered in a certain way to the nose and throat.

Take, for instance, the following case: Lady, fifty-six years old. Has been suffering the tortures of the damned for the last ten years or more. Constant, terrific neuralgic pains of top and sides of head. All sorts of numb, shooting pains behind ears, and radiating from nape of neck and occiput upward and forward over vertex; almost momentarily recurring hot flashes, despondent, morose, loss of memory; weak, extremely anemic,

under weight; cardiac arrhythmia. Gastric disturbances. Diagnosis: Paranasal sinus disease, especially sphenoidal and ethmoidal. All this due to a not completely deflected nasal septum.

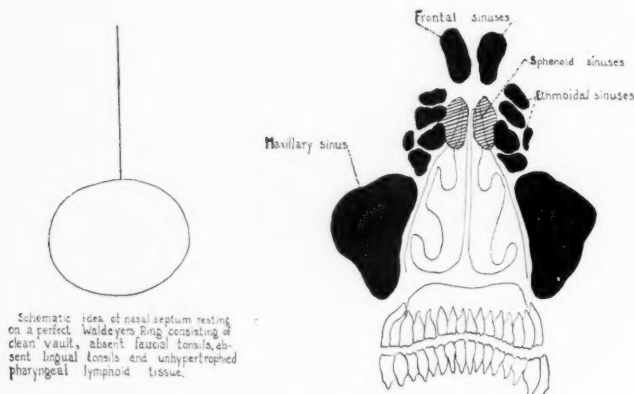


Fig. 123.

Patient's tonsils had been removed two years ago. About ten antisepticizing treatments to nasal fossæ proper, and prac-

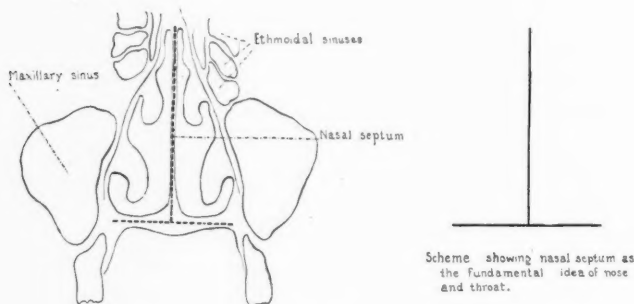


Fig. 124.

tically almost complete disappearance of all symptoms and patient happy. Advised correction of septal and turbinal entity.

These anatomic formations or, rather, malformations facili-

tate germ incubation exactly as in the properly protected test-tube or Petri dish. These anatomic formations need not necessarily be permanent. For instance, the formation of the nasal fossæ, nose, and throat (including the nasopharynx) may change from hour to hour or more frequently. Swelling of sections of the mucus membrane of the nasal septum, aided by swollen turbinate bodies, or parts of the turbinates, may exert all the detrimental influences of a truly and badly dislocated nasal septum. And yet, this is not a true or permanent deviation of the septum. It is a false, apparent, or temporary deviation, but producing just as much harm as a true deviation. We especially meet this condition in infants and very young children.

From earliest infancy the nose and throat are the first structures to be infected in practically all people. The immediate result of germ infection is swelling and displacement of tissue. This gives rise to two factors: 1. The interference with the proper intake of oxygen as regards quantity and quality. 2. The absorption of poison (toxins or germs) from the nose and throat areas inhibit the proper development of all the structures of the body, and particularly the more delicate bones of the head skeleton.

We are especially interested in the delicate bones to be found in the nasal fossæ, since they are constructed or erected into a mechanism for the production of disease. The breeding of germs is facilitated and made possible by this mechanism; and thereby a vicious cycle is established. We have this condition: the more germ-breeding in the nose and throat, the more is the nose and throat warped. And the more abnormal the nose and throat, the greater the amount of germ and toxin breeding, and hence the greater amount of bodily disease to be expected.

The one bone of all the body which has not as yet been given its due amount of importance in the vast field of preventive and curative medicine is the nasal septum. It is logically self-evident to the student of medicine that the nasal septum was always intended to be absolutely straight and very thin. The amount of human pathology that is directly and indirectly due to the deviated and thickened nasal septum is still a closed book

to the rank and file of medical men. The unsanitary manner of life under the civilized, communal form of living has resulted in a thickening and deflection of man's nasal septum. The explanation for this is extremely simple. And likewise the infinite amount of pathology this has been the principal direct or indirect agent in producing is equally clear. The definition of a perfectly normal individual, who will automatically remain well and disease free throughout a naturally long lifetime, is one possessing a perfectly straight and thin nasal septum surrounded by normally shaped, sized, and placed turbinate bodies, and the whole resting on a perfectly normal Waldeyer's ring. In other words, an anatomically perfect nose and throat which is always infection free. This, in time, will have to be accepted as true in our unceasing struggle for perfect health.

The nasal septum is one of the most delicate and important bones of the human body. Its vast and far-reaching influence is as yet very little understood. Around this partitioning structure we can build a romance of medicine. That this structure innocently lends itself to the production of a multitude of diseases is as yet incomprehensible to many. We will even have to accept the inevitable, and consider most common every-day ailments as originated by the essential assistance of this organ.

We will have to learn to look at the interior of the nose from the standpoint of the nasal septum. We will be compelled for the sake of logical, scientific accuracy to regard all the nasal fossæ structures with an eye to their relationship to the nasal septum. In other words, the septum is the primary structure, and all our reasoning and deductions must start from it and from here progress to the turbinate bodies, the sinuses, etc.

After all, what is of paramount importance is the cleanliness of the air we live in or the quantity that is actually absorbed by the lungs, or, rather, the quantity of oxygen that the body is capable of absorbing in any individual case. The explanation is simple. It can be stated in one sentence: It all depends on the type of nasal septum the individual possesses, modified by the type of turbinal entity, and whether this whole rests on an absolutely normal Waldeyer's ring. Another way of expressing

this idea is the following: We may correctly say that these abnormal factors prepare the body for invasion of the germ world. That is, the germs in themselves are incapable of doing all this harm, but once the body or parts of it are properly prepared, then the germs can do the rest.

Focal infection is nothing new. It has been going on for ages. Its method of procedure is new to us, and is, as yet, unknown to most of mankind. In every-day language it is merely a process of poisoning the body. This subject has two principal subdivisions.

1. What harm has it done the human body in all these thousands of years? What bodily changes has it brought about? This would come under degenerative changes to be found in the present-day human body.

2. What immediate harm is it causing the individual right now?

We will consider first the effect that focal infection has had on the pelvic bones of the mother. Focal infection and anoxemia interfere with the full normal development of all the bones of the mother's body. The pelvic girdle never develops as fully as it should, hence the danger of injury to the delicate nasal bones of the newborn.

The results of focal infection in the mother meet the infant as it is born into the world and these birth injuries in the newborn, caused by the pressure of the contracted maternal pelvis on the nasal septum, straining it, or more or less dislocating it to one side or the other, as it passes over a narrow pelvic outlet, later on produce in the nasal area ideal breeding places for germs, which gives rise to poisoning or focal infection of the individual for the balance of life. Simultaneous with this, the anatomic form of the normal channels, through which the body is supplied with oxygen, is permanently disturbed, and therefore the oxygen supply to the body can never be properly and correctly carried on, due to the distorted state of the nasal fossæ. These birth injuries only too frequently lay the foundation of the mechanism which produces ill-health. The breeding of germs in the nose and throat is facilitated by the formation

of numerous secret little spaces and, simultaneously, the proper oxygenation of the body is interfered with, all due to the distortion of the nasal fossæ. Hence we have the stunted, not fully developed pelvic bones of the mother (likewise caused by interference with full bone development in early life, and due to the same factors mentioned), causing injury to the child's nasal septum, which again is a heritage of disease for life. Just what percentage of nasal septums are injured at birth it is impossible to determine at present.

Those septums that are not injured or strained at birth have only the second factor to contend with throughout life. That is, thickening or deviations of the septum which are the result of direct poisonous absorption from the nose and throat areas, inhibiting the proper, full, normal development of the nasal septum which in its fully developed state was intended to be perfectly straight and thin. Another exception to this rule is the following: Direct trauma to the infant or child striking its nose in the act of falling while learning to walk or otherwise. This is another only too frequent cause for displaced and crooked septi as found later on in life. It is likewise impossible to determine at present what percentage of nasal abnormalities is due to this.

- The writer often describes the formation of the deviated nasal septum as follows: If the head is pictured as a box with a central partition representing the nasal septum, then the growth of the sides of the box—the bones that go to make up the face and skull—grow less rapidly, have their growth interfered with more than the partition of the box—the nasal septum—which grows more freely and easily, probably as a result of its thinness and also very likely because of the constant presence of irritation due to the ever-present nasal congestion; hence we have resulting the deflected septum. The inferior border of the nasal septum slips off the maxillary crest as a result of lack of room for growth and expansion and produces the ridge so commonly seen; or it may very often remain on the maxillary crest, but will flare out above, high up, either to the right or left, producing the high, more or less acute deflection of the nasal septum.

Hence, by various means, right here in the nose and throat we have erected a mechanism which constantly works toward the detriment of man. A distorted nose and throat, such as is found after all these factors have accomplished their evil results, interfere with proper oxygen supply to the body. And with the aid of what nowadays is commonly called focal infection or absorption this detrimental effect is brought about.

On careful study it is quite plain that this abnormal septal-turbinal-Waldeyer's ring entity principally accomplishes its evil, in a large percentage of cases, through the pathology that it originates in the paranasal sinuses, teeth, or both. The proper conception and appreciation of this thought is of the utmost importance. A crooked, distorted interior of the nasal fossæ, which as yet, unfortunately, so few men of the medical profession can recognize and properly understand, will give rise to and make possible germ breeding and incubation of the accessory nasal sinuses such as the sphenoid, ethmoids, or of the other sinuses, and from these locations send out their daily destructive poisons to almost any organ of the body. Thus, bad sinuses or teeth could not ordinarily exist without primary abnormality of the septal-turbinal-Waldeyer's ring entity. Hence we can very easily and logically trace infection of the sinuses as due to abnormality of the septal-turbinal-Waldeyer's ring entity. To make this plainer it must be remembered that an abnormal septal-turbinal-Waldeyer's ring entity is capable (*per se*) of originating pathology in adjacent or distant organs; but then again it is certain that this septal-turbinal-Waldeyer's ring entity or fractions of it make possible the origin of pathology in adjacent or distant organs by working through the paranasal sinuses or dental structures. What percentage is due to either is as yet unknown, and from the practical bases of actual practice it does not matter, as will be shown, when it comes to the important matter of disease prevention or cure.

There is only one other condition that competes with infection in the process of injuring man's good health. And that is tumor formation. New growths, cysts, etc., are the only other possibilities which we must constantly keep in mind as possibly

more serious and less easily remedial factors than focal infection. However, we should be thankful to say that they are extremely rare compared with the frequency of trouble due to the more benign focal infection factor. The latter can be found in almost everybody's case, whereas tumors are rare, especially in those under fifty. Ewing's theory of anaplastic cell growth helps materially toward shedding more light on this subject.

Therefore, if this nose and throat entity (septum-turbinal-Waldeyer's ring) is of such vast importance as regards the permanent welfare of the entire body, why can it not be looked at as the common foundation of good health? This it really is, and will be considered more so daily. It is the only way of which the writer knows to practice medicine logically, effectively, and scientifically. It is simplicity itself.

It causes what is commonly known as the lowering of the resistance or vitality. The thyroid gland undoubtedly has its function disturbed by this disease-instigating machinery and this ultimately leads on to actual pathology of the gland. This mechanism very often works in a fairly direct manner; for instance, on the middle ears, producing catarrhal or purulent, acute or chronic otitis. On the larynx, causing innumerable forms of laryngitis; on the bronchi, causing bronchitis. And so on, *ad infinitum*. On close analysis it undoubtedly works according to the old true principles of point of least resistance, which is really another way of saying the organ or organs subjected to the greatest strain, wear and tear, or to the most amount of usage in the struggle for existence.

And why cannot the same line of reasoning be extended to more distant organs, such as the stomach, etc.? The writer has only too frequently been convinced of this fact by actual cases in his daily practice, that, for instance, nothing will so quickly stop, control, and heal so-called ulcers of the stomach or the preulcerated stage as the removal of a set of infected tonsils, or further attention to the common foundation of good health or disease. This works fairly direct. The constant dropping of catarrhal secretions or even pus, which only too frequently is the case, sets up different forms of gastritis, or

infections of the other gastro-intestinal organs. This assists materially in giving birth to disease of different abdominal organs.

It is ridiculous to believe for one moment that it is only the organ complained of that is injured and suffering. If the above is true, every organ of the body is proportionately undergoing simultaneous injury to a greater or lesser degree. Hence we can see the fallacy of attempting to heal only the organ or member complained of. This is apparently the height of fallacy when considered in the above logical light. The only true, sensible course is to seek the original cause and eliminate that. In the majority of cases this can be done. If we permit the cause or instigating factors to remain, they will strike somewhere else next time, and in most cases it does not take long. Therefore most of the common, ordinary, every-day ailments or diseases are a hint that there are factors, working detrimentally, more or less constantly, to the harm of the individual. Hence we will be compelled to take a much greater interest in preventive medicine, and not merely confine our interest to the actual pathology present. This fact is true of most of our common, every-day ailments—almost anything.

A nose and throat, to be considered perfectly normal nowadays, must absolutely possess the following conditions, all depending upon and striving toward a perfectly normal Waldeyer's ring and normal nasal accessory sinuses, and particularly (and what is of the first importance) on the ability of the body to seize the necessary amount of oxygen as a result of the presence of a normal turbinal and nasal fossæ state:

1. It is necessary that the faucial tonsils be completely removed. The writer maintains and firmly believes that the tonsils cannot, under our present community life (in our present state of civilization), remain normal. All faucial tonsils are diseased. This is absolutely unavoidable under present living conditions. In every individual case they must invariably become and remain infected, and in most cases they become infected early in the person's career—in fact, in the earliest infancy—and remain so throughout life. The removal of the faucial

tonsils is a fundamental requirement in any attempt properly or permanently to relieve or correct the other important factors. It is utterly impossible to attain perfect normality of these factors unless the faucial tonsils have been completely removed. This is an essential. All nasal fossæ work is based on this law. It is the only proper foundation for building a normal nasal fossæ superstructure.

2. It is also essential for the general and special welfare of the individual that the lingual tonsils be absent, or at least that only the smallest amount of lingual tonsillar tissue be present.

3. It is essential that there be no visible lymphoid or follicular tissue about the throat proper (pharynx).

4. It is important that there be no adenoid tissue of any appreciable amount in the nasopharynx. This should be equally true of all adhesion bands and lymphoid tissue so commonly found in the vault of the pharynx.

5. It is essential that there be in the nasal fossæ a straight and thin nasal septum. This implies that all deflections, ridges, spurs, thickenings, etc., of the nasal septum, if present, be removed; likewise, that no other normal tissues be removed, and that no other foreign tissues be present in the nasal fossæ such as polypi, new growths, etc.

6. It is necessary that the middle and inferior turbinates be of normal size, that they hang freely in the nasal fossæ, and that none of them touch the external wall of the nose or the nasal septum. This is especially true of the middle turbinates, particularly that they be of normal thinness. The lower edges of the inferior turbinates should not come too far down, too close to the floor of the nose; that is, they must be a normal distance above the floor of the nose. Their lower margins should be at least $\frac{3}{16}$ inch above the floor of the nose.

7. The presence of normal accessory nasal sinuses is essential.

These seven conditions would presuppose normal accessory nasal sinuses. For the average case abnormal conditions of the accessory sinuses could not exist very long in the presence of these conditions. There would undoubtedly be a natural, spontaneous, automatic tendency toward a cure of any known

or unknown sinusitis which may be present in any nose which has been normalized to such a degree of perfection. The average case of sinusitis cannot persist very long after the institution of such perfect normality of the nose and throat as required by these conditions. With few exceptions the sinuses would automatically be freed of all diseases as a natural result of the institution of such absolutely normal condition.

The final and absolute test as to whether or not the individual's nose is perfectly normal after such work can be summed up in one word, mouth-breathing. Does the individual at any time during the twenty-four hours breathe through the mouth? And our ultimate goal and aim in all this work is the production of a mathematical equalization in every respect of the two nasal fossæ. What we must demand and attain is the ability to breathe through both sides of the nose in equal amounts and at all times. That is, to draw in and expel the same amount of air through each nasal fossæ simultaneously and continuously. This is the direct antithesis to mouth-breathing.

The sinuses are not to be regarded as the sole, guilty party in the causation of sickness and disease in infants, children, or adults. To consider them the sole culprit is false, illogic, and ineffectual; for the simple reason that such an attitude would presuppose that all we have to do is to attack the sinusitis and we have done all that is necessary.

There is one great fundamental fact which covers this subject of sinusitis and that is the following axiom: Sinusitis is directly capable of relief and cure in proportion to its length or duration or chronicity. This law controls the entire method and means of relieving and curing sinusitis, as will be shown. Above all things the following truism is to be remembered and constantly kept in mind. The nasal septum is the key to all the sinuses. And an axiom of this is the following: The nasal septum is the key to the sinuses, modified by the turbinal entity, and the whole controlled by the degree of normality of Waldeyer's lymphatic ring. Hence on these laws our method of attacking sinusitis rests. One thing, above all others, must constantly be remembered. The diagnosis, or determining exactly

which sinuses are involved, is as difficult as looking for the proverbial needle in the haystack. To overcome this difficulty it is not really necessary actually to determine just which and every single sinus that is involved. This is particularly true of early cases. It is enough if we determine the existence of sinusitis in the larger sinuses or in as many as we can, for we may be quite sure that we can never diagnose all of them, and furthermore it is unnecessary, as will be proved. It appears, on close study, that the principal source of systemic and local focal infection is derived mostly from two sets of sinuses—the sphenoidals and ethmoidals. The immediate effect of a distorted septum and enlarged turbinate bodies seems to be the clogging and interference with drainage and ventilation of the ethmoids and sphenoids. Hence, these two series of sinuses are to be blamed for most of our troubles.

From the point of treatment it is scarcely necessary to determine the exact sinus involved. The only exception to this rule is the maxillary sinus. If there is pus in the maxillary sinus, it should be opened and washed out frequently. Infection of all the other sinuses in both acute, subacute, and chronic cases are controlled by the septal deflection operation primarily, aided by the turbinal entity readjustment secondarily, and all controlled by the daily antisepticizing treatment to the nose and throat, especially to Waldeyer's ring. The rare exceptions to this rule are the cases of extremely acute, fulminating attacks of sinusitis which have to be treated as other acute abscesses, and, when possible, immediately opened.

In order to obtain mathematically exact results, it is absolutely essential that the work, both surgical and treatment, be carried out in a mathematically exact manner. There can be nothing slipshod about it; it must be done exactly and precisely. Patience and painstaking effort is the keynote. It is by far wiser to be overcautious, slow, and careful than hasty or careless. The writer believes in removing, under local anesthesia, one tonsil at a time and as little of the nasal work should be done at one sitting as possible. This is especially true of the very young, feeble, or old.

All operative work is to be preceded by the most careful of general physical examinations. This should include a careful urine analysis, blood-pressure determination, coagulation time, hemoglobin determination, etc.; a complete and full x-ray examination of all the paranasal sinuses and of all the teeth, and we should employ any and all other means which will give us a complete and thorough knowledge of the general condition of the patient for the sake of safety. I then prefer to give all my cases, when possible, from one to ten of my antisepticizing treatments to the nose and throat preceding any operative work.

By all means I prefer, wherever possible, to remove the patient's faucial tonsils as the first step in the undertaking to correct this common foundation of disease. This is done after the above mentioned course of cleansing and antiseptic treatments is completed and all the examinations and tests have been made, and we are sure the patient's physical condition can safely stand the strain of tonsil enucleation, nasal septal resection, or turbinal entity correction.

These above mentioned seven conditions, on close analysis, will be found to depend for their existence on the three fundamental cardinal factors. These are: First, diseased faucial tonsils with or without enlarged adenoids and bands. Second, the nasal septal state intensified by the turbinal entity. Third, the state of paranasal sinuses.

The foregoing is my definition of a perfectly normal nose and throat and I feel quite sure this will ultimately be accepted as a prerequisite to good health in general.

It is not to be forgotten for a moment that so much correction or reconstructive work, which is all operative, can and must only be undertaken with the greatest of care and thoroughness. The less one does at a time the better and safer will it be for the patient.

It should all be preceded with the thoroughness and care that any major piece of work requires. The preliminary physical and clinical examination must be done as thoroughly and carefully as possible. Nothing is to be left to conjecture or guesswork. Thoroughness and carefulness is the keynote of success

in this particular kind of work. In old and middle-aged people one tonsil only should be removed at a time. No work should be done on the turbinates simultaneously with the septal resection. One cannot be too cautious.

Last, but not least, it is absolutely necessary to possess healthy, infection-free teeth. That this is dependent on the possession of a normal nose and throat is too evident to require repetition. And what is of the greatest importance is the fact that no one can continue to possess or keep the teeth in a normal, healthy condition, even in the presence of a tonsil-free throat and a perfect straight and thin nasal septum, if sinusitis is permitted to remain. In other words, sinusitis, if allowed to exist, will ultimately destroy teeth. This sinusitis, in cases possessing a straight and thin nasal septum and an infection-free Waldeyer's ring, is undoubtedly due to abnormality in the turbinal entity. This latter factor gives rise to or, better still, continues the pernicious habit of mouth-breathing. This is the birth of the commonest vicious cycle. The more mouth-breathing, the more turbinal abnormality and hence more sinusitis and bad teeth. The following are axioms:

1. No one can possess good teeth unless the nose and throat are in perfect condition.

2. Good, healthy teeth cannot exist or continue to exist in the presence of a nose and throat that are abnormal (possessing one or more abnormalities). And, to make this more emphatic, I will state that no matter how frequently and how thoroughly the dentist corrects all dental defects in an individual mouth, they will return and continue to recur and extend as long as any abnormalities are present in the nose and throat.

3. To state an axiom dependent upon the two rules given above—the presence of bad teeth infer and are indicative of the presence of one or more abnormalities in the individual's nose and throat. Hence, if the nose and throat possess abnormalities, the individual must have, or will eventually have, diseased teeth or gums, or both.

And what is of the greatest importance—we must decide immediately, the moment we notice bad teeth or gums, decaying

teeth, pyorrhea, or apical teeth abscesses that the individual is afflicted with one or more abnormalities of the nose and throat, and the only way to stop the dental disease is to go back and eliminate the cause, which means removing the abnormalities from the nose and throat. This is all based on inductive logic of the simplest kind. Given a conclusion—bad teeth—why should we not be able to determine and recognize the premises—the crooked nasal septum, diseased sinuses, a poor turbinal entity, diseased tonsils or other abnormality of Waldeyer's ring or a combination of one or more of these factors.

Hence, we have ahead of us a vast field wherein we can apply this inductive logic. All cases of heart disease, kidney disease, and practically all other ailments of an infectious nature should be handled according to this light, which is direct, goes to and eliminates the cause.

The most cheerful and delightful thing the writer has worked out in this connection is what he calls a check-system on the accuracy of this method. He employs the method as a routine office practice or treatment in most every case. This is a general antisepticizing of the human being as far as we can go without surgery or injection. It is merely an antiseptic spraying out of the most intimate crevices of the nose and throat. It takes only a few minutes, is very direct in its results and obviates or delays operative procedures, especially in the feeble, old, or young. Take the following case: An elderly woman with an acutely inflamed, very painful, hard eye-ball, which had been operated on two years previously by one of our leading men for glaucoma. She receives the routine spray treatment, washing away the pus from her pussy teeth, washing out her filthy tonsils, and thoroughly cleaning out her nasal fossæ, and in two to three days the eyeball is white, and the tension begins to decrease from the start. The eyeball and head pains disappear within the first twenty-four hours. Pilocarpin and simple antiseptics were instilled in the eye.

My routine nose and throat treatment consists of an antisepticizing treatment and spray. I employ principally one solution consisting of the bichlorid of mercury solution varying in

strengths from 1 : 2000 to 1 : 5000. I employ this solution in the No. 56 DeVilbiss one-hole spray tip, since this tip, due to its smallness, lends itself to facile insertion into the various small cavities and areas, and can be carried back as far as the vault of the pharynx through the nose. It can readily be inserted into the crypts of the tonsils after thoroughly treating the teeth, pharynx, nasal fossæ, and epipharynx. I proceed in the following manner: 1. I gently spray the nasal fossæ with a mild anesthetic solution, using the No. 52 DeVilbiss spray bottle. 2. I then proceed to treat the throat and teeth. All the teeth-gum margins are thoroughly sprayed and all pus and other accumulations washed away. 3. I then proceed to the pharynx, the base of the tongue, and tonsillar crypts—these are thoroughly and quickly sprayed. Thus, all the rest of the surrounding lymphoid tissues of Waldeyer's ring is likewise carefully cleansed and antiseptitized, giving particular attention, in the case of adults and especially elderly people, to the lingual tonsils in whom such structures will almost invariably be found. In those cases wherein the tonsils have been removed we are spared the necessity of attending to them. 4. I then return to the nasal fossæ. By this time the anesthetic solution or this solution combined with adrenalin has had its effect and the nasal fossæ will be found wide open due to the contraction and shrinkage of the mucus membrane. Any mucus, pus, or dried concretions found anywhere in the nasal fossæ are removed by aspiration aided by cotton-tipped applicators, or forceps. The entire nose and throat area is thoroughly cleansed with the aid of suction. The two nasal fossæ are then thoroughly and carefully sprayed. The one-hole spray tip can be carried carefully and gently past the mesial surfaces of the middle turbinates, and thus the entrances to the sphenoidal fossæ are well sprayed. This is an extremely useful and important step, since, after all, sphenoidal and ethmoidal sinusitis are the commonest forms of sinusitis to be met with. The olfactory crevices and the external surfaces of the middle turbinates can likewise be thoroughly sprayed by this tip No. 56. All surfaces of the inferior turbinates and the vault of the pharynx are then well sprayed. All

this can be done in much less time than it takes to describe; in fact, it only takes a minute or two in the average case. The patient is cautioned to blow out and expectorate the excess solution, advising him against swallowing any. Too much force is not to be used in blowing the nose, and one side of the nose is blown at a time. In children and infants the tonsil suction apparatus is used to carry off the excess when treating the throat. The small quantity used to spray the nasal fossæ is left there, and need occasion no worry, since the amount is too small to be toxic. The writer does not infer that the solution he suggests is the only one to be used. He feels, however, that it has the advantage of cheapness and obtainability. He is not afraid of its toxicity when used in such small quantities. Any of the newer antiseptics could be used with almost the same efficiency.

An old man, seventy years of age, presents himself with an unusually severe infection of the conjunctiva of the right eye. The entire eyeball is intensely swollen, inflamed, and very painful. Inflammatory membranes cover the entire conjunctiva of both lids. This conjunctival condition is cleared up with the usual antiseptic treatment, but the eyeball is left in an intensely inflamed state with numerous extensive ulcers of the cornea. All sorts of antiseptic treatments to the cornea are of no avail, and iritis, then iridocyclitis sets in with increase in tension of the eyeball and the temporal and morning pains of glaucoma. The routine nose and throat and teeth treatment is now instituted, and the pussy, filthy teeth thoroughly cleansed; the tonsils and nasal fossæ washed out. The increasing tension of the eyeball is stopped. The pain of threatening glaucoma disappears, and in every way the eye is rapidly sent along the road to recovery.

Case I.—J. C., physician, sixty-one years old. In April, 1924 was taken with Jacksonian epileptiform convulsions of one-half of the body and attacks of unconsciousness lasting from six to eight hours. These convulsive seizures and attacks of unconsciousness came on more and more frequently; he would be

unconscious from two to four days at a time. After a great deal of medical examination by neurologists and internists of repute, he finally consented, at my urging, to have his septum corrected. Four years prior to this I had removed his tonsils. The septum operation and recovery followed without any unusual incidents, and as soon as the nose was in a condition to stand the pressure of the suction apparatus, it was applied, and thick, yellow pus was obtained from the right sphenoidal and ethmoidal sinuses. This was cleared up in a few weeks by the routine antisepticizing treatment of the writer, which makes it unnecessary to tear away and destroy the middle turbinate body. Repeated x-ray aid by Dr. Besser confirmed the existence, and final disappearance of the sinusitis.

The convulsions and all other troubles have disappeared and he has been conducting an active practice daily.

In passing, I wish to mention that the doctor had an old chronic, purulent middle ear, from which, he states, he has not heard in twenty years. At present this ear is dry, he hears the watch tick at a distance of 10 inches from the ear, whispered voice 20 feet. The antisepticizing treatments are continued (two to three times a week), in these cases for an indefinite period of time, until the drum is covered by a dry, thin, new, shiny drum, which invariably happens if the treatments are continued long enough.

Case II.—A. MacN., male, sixty-five years old, preacher. For years has been suffering and crippled with all the usual symptoms of generalized recurring attacks of articular rheumatism affecting most of his large joints and many of the smaller joints; patient compelled to use crutches; also considerable rheumatic iridocyclitis of both eyes, with resultant very poor vision. Treated routinely, nose and throat normalized surgically. This consisted of faucial tonsil enucleation, lingual tonsil removal, a complete straightening of the nasal septum, and normalizing the entire turbinal entity. The routine nasal spray, antisepticizing treatment was unintermittently continued during, in between, and for a number of weeks after the last oper-

ative procedure. Patient responded quickly and has been entirely well, active, and efficient in past six years; vision excellent in both eyes.

Case III.—E. K., female, age seventeen years; family history negative. The usual mild diseases of childhood, with the exception of chorea, which disease affected the patient throughout a period of two years or more of her early childhood. At this time, apparently, no heart, lung, or other organic trouble discoverable, either on examination or by history. Faucial tonsils and adenoids removed by writer eight years ago. Chorea gradually disappeared and patient was well up to one year ago, when she noticed increasing dyspnea, especially on slightest exertion; rapid loss of weight, loss of appetite, weakness, constant chronic temperature of 100° to 101° F.; pronounced irritability of temper, aroused to anger on slightest provocation; general mottled condition of skin of face and limbs. Physical examination disclosed cardiac murmurs, undoubtedly mitral, systolic and diastolic in time, which are ordinarily found present in the ordinary rapidly discompensating heart. Apex beat greatly displaced to the left.

The patient had a decidedly bad deflection of the nasal septum, high up to the right and almost completely blocking the upper and posterior two-thirds of the right nasal fossæ, with external displacement to the left at the tip of the nose of the anterior tip of the triangular septal cartilage. There was a complete approximation of the upper right area of the septum to the right middle turbinate, compressing it completely against the external wall of the right nasal fossæ, thereby interfering with drainage and ventilation of the right frontal and anterior ethmoidal sinuses and, likewise, interfering with drainage and ventilation of the right posterior ethmoidal and right sphenoidal sinuses. The left middle turbinate was one immense mass of ethmoidal cells that had undergone compensatory enlargement merely to fill up the large empty space in the left middle section of the left nasal fossæ, due to the decided deflection of the nasal septum to the right. The writer performed a com-

plete submucous operation, including correction of the displaced piece of triangular cartilage, at the tip of the nose. The left middle turbinate was compressed with a pair of forceps to the thinness of an ordinary middle turbinate. The right middle turbinate was fractured at its base (infracture), and reset about $\frac{2}{16}$ inch from the external wall of the right nasal fossæ.

The patient made a rapid, uneventful recovery from the above operation. A profuse, continuous, mucopurulent nasal discharge, which had been affecting the patient for quite a long time previous to the operation, gradually began to disappear immediately after the operation. Within a few weeks it was entirely gone. However, one point of the greatest importance and interest was disclosed very shortly after the submucous operation. On applying the suction apparatus to the nasal fossæ, a profuse amount of thick, white pus was obtained, flowing down rapidly from the right posterior ethmoidal sinuses. Within the next three weeks this discharge of pus also disappeared and was no longer obtainable with even the strongest amount of suction. Due to the fact that the septal deflection was complete, the presence of free-flowing pus from the posterior ethmoidal or sphenoidal sinuses was invisible to the eye, even on the application of the strongest amount of suction.

The patient's general symptoms rapidly commenced to disappear simultaneously with this nasal work. All dyspnea, even on walking and moderate exertion, completely disappeared. The mottled, blotchy, purplish condition of the skin of the nose, cheeks, face, and the lower extremities also rapidly disappeared. The chronic temperature of 100° to 101° F. was no longer obtainable. The irritable, fretful, nervous disposition was replaced by a normal, cheerful smiling one. The patient returned to her more than normal weight of 112 pounds. The heart murmurs in the space of a few weeks reduced themselves to a strong systolic and fair diastolic. Otherwise the previous confusion and mumble of cardiac murmurs had disappeared.

The patient has returned to work and does not tire easily, even under a fair amount of exertion, and neither this nor a moderate amount of walking cause any recurrence of dyspnea.

Appetite is good; sleeps well; constipation is no longer complained of. It is impossible to enforce the necessary amount of rest in such a patient, feeling as well as she does. This patient has a perfect set of teeth.

In the last few weeks the systolic murmur has shown a tendency to disappear. The diastolic murmur, however, is as persistent and loud as ever. Menstrual history, which previously was quite irregular, profuse, and bimonthly, now is monthly and otherwise normal.

Case IV.—F. McC., female, age twenty-one years. History of repeated attacks of acute articular rheumatism dating back quite a few years. Most joints of small bones are stiff, and in many decided limitation of motion present. Some of the vertebral and also one hip-joint affected with limitation of motion. History of tonsillectomy at age of fourteen years. Heart, lungs, urine, negative. Patient's chief nose and throat complaint at this time was a constant and annoying postnasal (epipharyngeal) catarrhal dropping. Throat examination presented a normal appearance aside from a small tongue of tonsillar tissue protruding from behind the right anterior tonsillar pillar. This piece I removed subsequently in my efforts to relieve the patient of the annoying postnasal catarrhal droppings and, to my surprise, I found that it led me down to a large mass of tonsillar tissue, which unsuspected, has been buried behind the anterior tonsillar pillar and in the depths of the throat. The nasal fossæ presented a decided high, acute deflection of the septum to the right, touching a rather large anterior tip of the right middle turbinate, whose outer surface again was entirely too close to the external wall of the nasal fossæ, thereby interfering with drainage from the right frontal sinus and right anterior ethmoidal sinuses.

The writer corrected the septal deflection by a complete submucous operation. There was a decided improvement in the patient's general health and a pronounced diminution in the amount of catarrhal droppings as a result of the above operative interference. The patient continued to improve in

strength and health, with great relief from the rheumatic attacks, for about two years, when suddenly one morning I was hurriedly called to find an acute purulent frontal sinusitis (right side) with almost completely closed right eye, due to edema of the inflammatory swelling caused by the sinusitis. Severe pain and tenderness was present over the right supra-orbital ridge and adjacent area of the frontal bone. The interior of the right nasal fossæ presented patent pus flowing down from the right frontonasal duct. The anterior half and tip of the right middle turbinate was greatly enlarged, occluding the frontonasal duct, this interfering with the drainage and ventilation of the right frontal sinus. I compressed the right middle turbinate and fractured its attachment at its base to the ethmoidal bone. A small pledget of absorbent cotton was inserted between the ethmoidal bone and the middle turbinate. The turbinate was not removed. Within the next few days the patient developed an attack of acute parenchymatous nephritis, with edema of the extremities, facial swelling, and the usual urinary findings were reported. This nephritic attack ran its course in a few weeks to complete recovery, including a normal urine. The patient is today in excellent health, possessing a normal nose and throat.

Case V.—P. T. C., male, fifty-two years old, has for the last three years been unable to work, due to the fact that he has been suffering with all the incapacitating and lamentable symptoms of a nervous breakdown. Physically, otherwise normal. I treated him routinely for a short period. His common foundation of good health was then corrected, which included a complete removal of his faucial tonsils; and at a safe interval this was followed by a thorough nasal septal correction, so that he was given a perfectly straight and thin nasal septum. Then all his turbinate bodies were normalized from the standpoint of size, position, and shape. The routine, antisepticizing treatment was employed throughout all this time and continued for some time after the last operative procedure. In the past five years he has been fully efficient in every way and has not lost a day from work.

Case VI.—Girl, twelve years old, underweight, undersized, and poorly nourished. Suddenly developed a left-sided, complete, facial paralysis, unable to close left eye, and profuse annoying epiphoria. Patient had an incomplete tonsil removal a few years ago. Patient's nasal fossæ in a very poor state, due to considerable sphenoidal and ethmoidal sinusitis, undoubtedly brought on and caused by the presence of a decidedly deflected septum and poor turbinal entity. These abnormal factors compelled the patient to be a mouth-breather. Patient otherwise normal. Patient's nose and throat treated routinely; facial paralysis disappeared by end of third week. Advised correction of septal deflection and turbinal entity. Remains of tonsillar tissue was removed by writer.

Case VII.—Male, forty-seven years old. Police captain. *Past history:* For a number of years has been a chronic sufferer with the severer forms of rheumatism. His right eye was severely affected and iritis, iridocyclitis, and secondary glaucoma followed in close succession, resulting in total blindness to this eye and uncontrollable symptoms. Enucleation was the only relief. *Present history:* Patient came to me with fairly advanced symptoms in left eye, which were very similar to those he experienced at onset of trouble in right eye. I treated him routinely, enucleated his tonsils. All eye symptoms disappeared, and he has been active and well for past seven years.

Case VIII.—Mrs. J. M., age thirty-seven years, mother of five children. *Past history:* Suffering for years with eczematous-kerato-conjunctivitis, numerous phlyctenules covering both cornea. Likewise afflicted with chronic blepharitis of both eyelids of each eye. Patient treated routinely as outlined, and operated by writer six years ago for complete tonsil removal and complete submucous resection of nasal septum. Patient improved rapidly, phlyctenules disappeared, eyes cleared up completely. Patient disappeared from observation for six years or more. Returned in March of 1925 complaining of pain over right mastoid and pus discharging from right ear. Watch

tick not heard on this ear, whispered voice heard at $1\frac{1}{2}$ feet only. Writer removed large, dangling polypi from underneath left middle turbinate (left anterior ethmoidal sinusitis and double sphenoidal sinusitis confirmed by x-ray). Patient went home and disappeared from treatment for two days, when writer was hurriedly called, and found patient flat on back, unable to raise her head, and suffering with all the acute symptoms of an acute attack of serous labyrinthitis, such as extreme tinnitus, vomiting on elevation of head, a marked right horizontal nystagmus on directing patient to look to left, and continual sensation of room and all objects in it constantly turning around. Patient extremely dizzy on slightest motion. Marked pain, tenderness, and swelling present over right mastoid.

Patient placed on Dover's and aspirin and treated routinely, twice daily. Right ear also cleansed with same spray solution, and canal filled with bichlorid of mercury solution (1 : 2000). All symptoms rapidly commenced to ameliorate, and under the continued use of the writer's simple antisepticizing treatment the patient was up and about, and all symptoms, including pain, tenderness, and swelling over mastoid process, had disappeared by end of fourth week. Hearing normal to all tests.

The reason for the recurrence of trouble in the above case is easily explained. The patient's turbinal entity had never been completely normalized and she had remained a mouth-breather all her life. Recurrence of infection of the nasal fossæ was inevitable, and its spreading to the sinuses unavoidable in nasal fossæ afflicted with such turbinal distortion. The spreading of the infection from the sinuses to the ear was the next step.

As a rule, the gum margins are simultaneously infected in these cases. This was proved to be true in this case. The patient never returned to perfect nasal breathing and mouth-breathing was ever present; hence we have the continuance or exacerbation of the sinusitis, and then the acute ear condition; the infected state of the teeth-gum margin is likewise due to this state of affairs. This must be attended to and the pernicious mouth-breathing habit stopped.

The most depressing thought of all is the fact that just when most successful men reach their greatest stage of usefulness to their fellows they die from some condition which, in the majority of instances, is due to this combined factor of constant poisoning (focal infection) and anoxemia. This has been operating for many years in each case. In other words, they are destroyed by preventable conditions which could easily have been eradicated and this unfortunate, too early collapse, prevented. Hence, this untimely death was unnecessary and preventable. Can one imagine the amount of suffering, inconvenience, and annoyance they had to put up with, throughout all the years, until they were carried off.

The automaticity of the mouth-breathing habit is almost startling in its exactness. The individual breathes through his mouth in direct proportion to the amount of abnormality existing in his nose and throat. And as the amount of pathology or abnormality of the nose and throat is removed, just to that degree will the mouth-breathing habit be discontinued and normal nasal breathing be resumed, which is, after all, the only proper manner in which to breathe, and the only way in which the air can be properly prepared by the turbinal entity for reception by the lungs, and thereby enabling them to absorb a safe margin of oxygen for the bodily needs of protection and nourishment. The air must be so prepared that the alveolæ are capable of absorbing the necessary normal amount required to maintain the highest degree of resistance and permit the body chemistry of nutrition, elimination, etc., to be carried on to the correct degree.

It is the writer's ideal to save and spare, as much as possible, the turbinate bodies, since a normal turbinal entity is so essential in maintaining perfect good health. Whole turbinate bodies should never be destroyed unless absolutely necessary to save life. These instances are rare. The turbinate bodies are absolutely necessary physiologic organs as essential as other normal functioning organs.

It is not at all well for the profession or humanity to leave, overlook, or permit to remain the causes that produce so much

and varied pathology of the human body. Tuberculosis of any organ means that the instigating factors that have caused the tuberculosis exist in the nose and throat. And the same logic can be applied to most of man's illnesses and diseases. Pneumonia in an individual means that that person's nose and throat is at fault, and these faulty factors have permitted the pneumonia to supervene. And thus we can and must reason throughout almost the entire gamut of diseases that man is heir to. We will be compelled for our own self-respect and for the dignity and respect we owe the profession of medicine to seek out and remove these instigating factors. If we allow them to remain, they must sooner or later cause other diseases or disease of other organs, until finally they lead on to man's complete dissolution. We will be doing more for humanity. In fact, to only too happy and great an extent we will be doing just what humanity wants us to do. Can one realize the amount of respect this will command from the average person? The fact that it will decimate, or even cut down to a twentieth or even to a smaller amount the quantity of medical practice means nothing. The profession of medicine is inherently a self-eliminating one. Does one realize the amount of surgery this will prevent; and the tremendous number of medical cases that will never happen, thanks to this method?

And the above explains, quite rationally, just why the nose and throat man is to so great an extent taking the place of the general practitioner. It is not that the usefulness of the general practitioner is gone, but that he has become more efficient. He is simply assuming a new name as a result of the new and more efficient methods he is using. This is a necessary and good transition period of the times.

That the human being is capable of standardization is a foregone conclusion. And when considered in the light of the above we can readily see how correct and logical this is. One would think it is an extremely difficult matter to standardize the race, but this is not so, and on careful study we will have to admit it is a very simple thing. In fact, it is very necessary for the sake of accuracy and peace of mind that we do regard it in this

light. The haphazard, hit and miss days of the practice of medicine are doomed to disappear very quickly, to the greater dignity and respect of the field of medicine generally. Undoubtedly, these methods and remedies outlined above are drastic, but, after all has been said and done, they are the inevitable. But it has been truthfully said many thousand of years ago that by the sweat of our brows shall we earn our bread. To accomplish anything worth while is painful, and the more important the result to be attained the more pain required.

That this will be a new system of medicine is apparent to even the casual observer. The writer can only contemplate a logical, accurate, effective medical science, when considered from this standpoint. Of course, it is a man's medicine. It is not for the timid. The ridicule and approbium that has been heaped upon the medical science will only then disappear. The various pseudomedical sciences and cults will be shown up in their truly ridiculous light.

Summary.—One inquires what is to be done about it all? What a tremendous amount of reorganization we will have to go through. It will all have to go back to the colleges for proper and careful lucid teaching to the student body. This is absolutely necessary for the good and welfare of the race and human family. I can already visualize each and every community and town and city having one or more special institutions exclusively devoted to the correction of this common foundation of good health or disease—these places maintained and run by the public.



CONTRIBUTION BY DRS. I. W. HELD AND
IRVING GRAY

PRESENT STATUS OF x -RAY DIAGNOSIS OF GASTRIC
AND DUODENAL ULCER

x -RAY diagnosis of ulcer of the stomach and duodenum has been subject to the same fate as the clinical diagnosis of this disease. In fact, it may be said that up to the surgical and especially to the x -ray era of diagnosis of ulcer of the stomach this disease was diagnosed more often than it really existed. This explains why the literature is so rich in reports of cures of gastric ulcer. No doubt that in no small percentage of those cases there was no ulcer. The clinical diagnosis of duodenal ulcer, on the other hand, was but very seldom made unless perforation or hemorrhage occurred.

The x -ray diagnosis of gastric ulcer likewise gained in interest long before that of duodenal ulcer, as demonstrated by the fact that until 1910 most contributions to the x -ray literature of ulcer were entirely devoted to gastric ulcer. Even in 1911, when E. Schlesinger so strongly advocated x -ray diagnosis of duodenal ulcer by indirect Roentgen signs, his contribution was received with great skepticism. It is to the credit of the American and English schools to have swung the pendulum and to have disclosed the true condition of affairs. Moynihan in England and the Mayos in this country demonstrated beyond any doubt that duodenal ulcer is much more frequent than gastric ulcer, a fact universally accepted today. L. G. Cole was the first to demonstrate roentgenologically duodenal ulcer by directly visualizing the seat of the pathologic changes. The French and the German schools, being rather followers than originators in the diagnosis of duodenal ulcer, have long minimized the importance of differentiating gastric from duodenal ulcer, both

clinically and roentgenologically. They have tried to evade the term "duodenal ulcer" by speaking of postpyloric, dextrapyloric, and juxtapyloric ulcer. These terms have now been almost entirely abandoned, and it is universally recognized that clinically, roentgenologically, and surgically gastric and duodenal ulcer are separate entities. Cole still speaks of duodenal ulcer as postpyloric because he considers the first portion of the duodenum to be part of the pylorus. This view cannot be shared by the authors for reasons to be explained in another part of the article.

There is uniform agreement that the direct Roentgen visualization of the pathologic lesion in the stomach and duodenum is the most important guide in the diagnosis. It cannot be denied, however, that ulcer of either stomach or duodenum may be present without revealing any roentgenologic manifestations pointing to the seat of the ulcer. It might be well at this point to call attention to the fact that many patients after an "ulcer cure" may subjectively feel quite comfortable, while the x-ray examination may show findings similar to those present before treatment was instituted. Barsony and Szemzo report several cases of bulbus deformity after an "ulcer cure." It is well known that cases of duodenal or gastric hemorrhage, x-rayed a few weeks after active bleeding, may reveal a perfectly normal stomach and duodenum. It is true that there are many sources for gastric hemorrhage other than a gastric or duodenal ulcer, but there is no doubt, however, that the greatest majority of all the cases of hematemesis or melena is due to either ulcer of the stomach or duodenum or cancer of the stomach. It is also known that in a great number of cases where there is a definite history of ulcer of stomach or duodenum, the x-ray is negative as far as direct visualization of the ulcer is concerned. C. Ruhnenfuhrer, in 24 positive gastric ulcer cases diagnosed by gastroscopy, reports only 8 had positive x-ray evidence in the form of niche.

It must, therefore, be emphasized that the direct signs of ulcer, as valuable as they are, are only encountered in the minority of cases, and that in addition to the direct signs the

proper evaluation of the indirect signs is indispensable. The interpretation of direct signs is very simple. The evaluation of indirect signs, on the other hand, requires a great deal of experience and can only be properly interpreted in connection with the other clinical symptoms. There is hardly an indirect Roentgen sign of gastric or duodenal ulcer that may also not be present in another intra-abdominal disease or even in functional or metabolic diseases. The proper interpretation of the indirect signs is just as much a matter of experience as the proper interpretation of the subjective symptoms and clinical history. In our diagnostic training it is much easier to learn objective signs like murmurs, the palpation of tumors, than it is to learn how to properly interpret subjective symptoms. It is, therefore, reasonable to compare the direct signs to the objective findings, and the indirect signs to the subjective complaints of the patient. Most of the direct Roentgen signs always persist to a lesser or greater degree irrespective as to whether patient has symptoms or not, while the indirect signs are only present during the state of symptoms depending on the secretory, motor, and sensory disturbances caused by the ulcer.

In view of the fact that the patient usually presents himself for examination during the active symptoms, indirect Roentgen signs are present in a great many cases and are of diagnostic value. It will be shown below that many Roentgen signs which point directly to the seat of ulcer may also be of transient nature.

ROENTGEN DIAGNOSIS OF ULCER OF THE STOMACH

In view of the fact that the direct signs are more important, they will be discussed first.

Niche.—Hemmeter was the first to have observed the lodgment of bismuth in the ulcerated area. Based on this he suggested the possibility that the diagnosis of gastric ulcer will be simplified by the fact that the contrast (in his case bismuth subnitrate) would stick to the ulcerated area. It is more than likely that the case of Hemmeter was actually the first visualization roentgenologically of a niche.

In 1909 Reiche was the first to observe the protuberance

on the lesser curvature, roentgenologically, but to Haudek belongs the credit to have properly interpreted the findings of Reiche, and he named this protuberance "niche." At about the same time the late Faulhaber independently brought to our attention the diagnostic importance of the "niche."

The most common localization of the niche is on the lesser curvature just above the angulus which is about four finger-breadths away from the pylorus. The niche may appear either like a small projection in which the upper line is horizontal and the lower line oblique, or there may be a short distance between the ulcer and the stomach wall. The ulcer is not on the lesser curvature, but somewhat on the posterior wall. As we approach the pylorus the frequency of ulcer increases, whereas the frequency of the niche decreases. The factors of static and mechanics are probably responsible. In order for the niche to appear the ulcer must extend at least to the muscularis mucosa. An ulcer can be large, but if the mucous membrane only is involved, no niche will be seen. The contraction of the muscularis mucosa is responsible for the picture of the niche. It is not rare to find this direct evidence of an ulcer in the morning, and later in the day, when the muscle spasm relaxes, one may obtain the picture of a normal stomach. The niche has disappeared even though the ulcer is present. It is important to be cognizant of this fact because false conception and false conclusions may be drawn simply upon the presence or the absence of this direct sign—niche.

As the ulcer continues to invade the muscular tissue the niche becomes larger, due to the muscular tissue contraction around the ulcer. The irregularity of the niche does not speak for malignant degeneration of the ulcer, for an associated perigastritis may be responsible for the deformity on the lesser curvature.

The secondary changes consequent to the niche formation may be either functional or organic. The niche is much less frequently situated on the lesser curvature in the prepyloric region. Its location on the posterior wall is very uncommon and on the greater curvature it was first observed by Schinz.

The pathologic changes in the ulcer which cause the niche vary. In most cases it is caused by a callous indurated ulcer reaching the serosa and often even breaking through the serosa into the neighboring organs, pancreas, liver, spleen, omentum, etc. The size of the niche may vary from a pea to that of a large hazelnut and even a walnut. Some observers are of the opinion that an excavation on the lesser curvature, 3 mm. in diameter, suffices to bring about the Roentgen manifestations of a niche.

In some cases even the simple ulcer on the lesser curvature in which only the mucosa and part of the muscularis are involved, as stated above, gives rise to the formation of a niche. In the latter case the niche is caused, as rightfully pointed out by Reiche, not so much by the excavation as by the increased intra-gastric pressure. This explains why the niche of a simple ulcer may be present at one examination and disappear at the next examination, even if only a few hours apart. In other words, it may be said that the niche caused by the simple ulcer is a pure pulsion diverticulum, whereas, that caused by the callous and penetrating ulcer is both a pulsion and a traction diverticulum. The pulsion diverticulum is to a certain extent the expression of a functional disturbance of the stomach as the result of ulcer, whereas the pulsion and traction diverticulum of the callous ulcer is the expression of a permanent change, the latter is present both during the time of ulcer symptom and when there are no symptoms. It is the pulsion diverticulum that has led some observers to the assertion that every niche can be cured by medical treatment. This kind of niche in reality may yield to treatment, but the optimistic reports of Ohnell, Hamburger, Einhorn, Diamond, and others must not make us forget that the niche due to the penetrating ulcer has in most cases such destructive underlying pathologic changes that fatal perforation, hemorrhage, or destruction of the neighboring tissues by slow perforation, as chronic pancreatitis, hepatitis, encapsulated pus formation in the neighboring omentum, may result, if we allow the opinion to gain ground that every niche can be treated medically. That a niche may exist, not being visualized roentgenologically, has been proved by a case reported by Edward

Hollander. In his case one examination showed, roentgenologically, the presence of a niche, and repeated after examinations failed to show it. The operation, however, revealed the presence of a callous ulcer on the lesser curvature. Hollander explains the failure of the niche to have filled with contrast substance because of a mucous plug filling the neck of the niche. It is important to mention that some of the cases reported in the literature as having healed based on the disappearance of the niche had to be operated shortly after they were pronounced cured. One of the cases known to us which was pronounced cured succumbed to hemorrhage six weeks after.

We may therefore speak of two forms of niche: one equivalent to pulsion diverticulum on the basis of simple ulcer which may justify medical treatment, and another, pulsion and traction diverticulum, necessitating in the majority of cases surgical intervention. A few remarks as to the technical requirements for the localization of the niche may be in place. Fluoroscopy and plate taking are essential. The patient should take the contrast meal while he is being observed fluoroscopically. In that way the filling of the niche may best be detected. The different parts of the lesser curvature should be screened off in order not to overlook a small niche, and the entire lesser curvature should be palpated carefully, as in this way the contents may at times be forced into the niche. The Holzkecht spoon is often likewise of great aid in filling the niche. The patient should be turned to the left and right side, and be examined also in the ventrodorsal position. The examination, however, is not complete unless the patient gets a suspension of contrast substance and allowed to lie on his back in order not to miss the filling of the niche on the posterior wall. Roentgenograms should be taken of the stomach in the same position in which the niche was best visualized fluoroscopically.

The niche caused by a simple ulcer (pulsion diverticulum) is usually semiglobular, the base being situated on the lesser curvature. It empties when the rest of the stomach is empty. It is regular in outline (Fig. 125) and is never larger than a small hazelnut, usually smaller. There is at times spastic in-

dentation on the greater curvature opposite or slightly above the site of the niche, which is also only transient, and is more often present in vagotonic than in normal individuals. The rest of the stomach is usually perfectly normal in outline. The lesser curvature is not shortened. At times there are teeth-like contractions on the greater curvature which were at one time considered to be due to spastic contractions (Groedel). Forssell rightfully interpreted these teeth-like contractions to be due to contrast lodging in the folds of the mucous membrane. Careful study of the roentgenograms also shows in these cases as first pointed out by Lenk and Eisler that the rugæ of the mucous



Fig. 125.

membrane in the immediate vicinity of the niche do not run parallel, but converge from the seat of the ulcer. The motility of the stomach with a niche due to simple ulcer is, as a rule, never disturbed. In reality, there is pyloric insufficiency with rather hastened emptying of the stomach analogous to duodenal ulcer. This observation was made by Fr. Kraus and independently by Held and Gross. At times reflex late pylorospasm like in duodenal ulcer causes delay in emptying of the stomach—the so-called paradoxical rest.

The niche due to callous and penetrating ulcer (pulsion and traction diverticulum, Fig. 126) is usually much larger. The base is often narrower, due to connective-tissue formation,

causing sometimes a distinct neck. This neck may be so narrow as not to allow the contrast meal to enter the niche or to fill only part of the niche, making it appear smaller than it in reality is. This explains why the surgeon may sometimes find a niche which was not demonstrated by *x*-ray, or he may find a much more extensive invasion of the lesser curvature than was seen roentgenologically. Cole pointed out that in the interpretation of an excavating ulcer one must not only expect the budding appearance of the niche, but also the flattening around the protrusion. The shape of such a niche may vary. It may be circular, semicircular, and quadriangular with irregular borders.



Fig. 126.

If the niche penetrates into the pancreas it does not move with respiration, if the niche penetrates into the liver it does move with respiration. It may sometimes be so large as to correspond to a palpable mass simulating cancer. At times there is a vacant longitudinal space between the lesser curvature and the niche, giving the impression as if the shadow representing the niche does not belong to the stomach. If the patient is carefully turned from side to side while fluoroscoping, it can be determined that the niche belongs to the stomach. The pars media in these cases is often deformed, resembling an organic hour-glass due to the changes in the wall of the stomach, and there is often a

very marked persistent indentation on the greater curvature opposite the site of the niche (Fig. 127).

In this form of niche the part of the stomach below is considerably dilated, atonic, and there is marked delay in emptying, sometimes simulating pyloric stenosis and suggesting the diagnosis of a double callous ulcer, both of pylorus and on lesser curvature. In reality the delay is not due to a callous ulcer of pylorus, but to the loss of tone and to the extensive destruction of the involved part of the lesser curvature, interfering with the normal innervation of the stomach.



Fig. 127.

It is known that the stomach receives its nerve supply from the vagi and from the sixth, seventh, eighth, and ninth dorsal segments of the spinal cord. The nerves coming from these dorsal segments are composed of sympathetic fibers that reach the stomach through the splanchnic nerves, the sixth dorsal segment supplying the pylorus. In the stomach wall we find one nerve plexus in the submucous coat (Meissner), and another nerve plexus in the muscular wall (Auerbachs). In 1911 Cannon, *Mechanical Factors in Digestion*, described the so-called myenteric reflex. This term he used to designate

the intrinsic response of the gut to stimulation by its contents in order that normal progression in proper fashion takes place. The innervation of the lesser curvature is of great importance in the proper propulsion of food. That extensive involvement of the lesser curvature by ulcer influences anastalsis is proved by the fact that patients so afflicted vomit much more frequently than if the ulcer is situated in any other part of the stomach.



Fig. 128a.



Fig. 128b.

In addition to the niche caused by callous ulcer, Haudek also speaks of a niche that definitely points to a penetrating ulcer, which is characterized by the fact that it contains, in addition to the contrast substance, also a bubble of gas (Figs. 128a, 128b) and that it remains filled after the rest of the stomach is emptied.

The diagnosis of penetrating ulcer should not be based on the presence of the bubble of air in the niche as the niche described above (pulsion and traction diverticulum) is, in reality, in many cases due to penetrating ulcer, although it contains no gas bubble. A diagnosis of penetrating ulcer of lesser curvature would be much more rarely diagnosed than it is surgically en-

countered if it depended only on the presence of a gas bubble in the niche. At times cases are seen where only gastric secretions and a gas bubble are seen in the niche. Sometimes three layers may be seen in the niche, the contrast substance, the secretion, and the gas bubble.

There are a number of conditions which may simulate a niche as, for instance, a loop of small intestine overlying the lesser curvature or a peristaltic wave over the lesser curvature bulging out prominently. A mistake can be easily avoided if the patient is observed fluoroscopically sufficiently long. At times calcified tuberculous glands in the region of the lesser curvature may simulate a niche to such an extent as to even cause surgical intervention. A. Bassler and J. R. Lutz rightfully called attention to the fact that a niche on the lesser curvature is frequently erroneously diagnosed, and these cases are later demonstrated as a proof of medical cure. It is, without question, a very useful caution. E. Schlesinger and DeQuervain described the so-called functional gastric diverticulum manifesting itself by a projection on the lesser curvature containing contrast substance, secretion, and a gas bubble, thereby fully resembling a penetrating ulcer, and the operation failed to reveal its presence. Cholelithiasis was present in the 2 cases quoted by DeQuervain. In Schlesinger's case there was a duodenal ulcer. In 1 case DeQuervain observed during the operation a projection of the gastric wall, if he exercised slight finger percussion on the stomach. He, therefore, concluded that this diverticulum is due to a peculiar innervation disturbance of a local part of the gastric wall. Akerlund, based on postmortem examination, later interpreted correctly this so-called functional niche. His case showed that there was in reality an organic diverticulum, but not of the stomach; it was due to a dilatation of pars inferior duodeni at the junction of the jejunoduodenal flexure which on account of its location simulated a niche on the lesser curvature. Such a mistake ought to be avoided if the patient is examined fluoroscopically in different angles and during different times.

The view has often been expressed by L. G. Cole and others

that a larger sized niche is an indication of ulcer having undergone carcinomatous changes. It is not safe to be guided by the size of the niche as to whether it is due to a callous ulcer or to malignant degeneration.

R. D. Carman described the Roentgen manifestations of an ulcer having undergone malignant degeneration. He says if the ulcer is on the vertical wall of the lesser curvature or on the posterior wall near the lesser curvature, it appears as a dark slightly crescentic shadow of barium filling the crater. The convexity of the crescent is toward the gastric wall, and the concavity toward the gastric lumen resembling a meniscus. If the ulcer is on the lesser curvature distal to the incisura angularis, the concavity of the meniscus is toward the gastric wall. On the posterior wall it is brought out by a stroking pressure, as a circular dark shadow surrounded by a lighter zone. Another characteristic feature of this type of niche is the overhanging edges which prevent its emptying when the rest of the stomach is empty. The size of the ulcer is at least from 3 to 8 mm. in diameter.

If the niche is associated with carcinomatous degeneration of the stomach, the pars media is much more deformed and the lesser curvature in the region of the niche is rounded out, showing a definite defect, and the area involved shows no peristalsis. This is so striking that a mistake in the diagnosis can hardly be made.

If a niche is situated in the prepyloric region it is much more difficult of diagnosis because of active peristalsis in this area. This subject is more fully discussed in another part of this article. If the niche occurs near the cardia, one may be able to locate it by having the patient lie on his back in the oblique position (Levy-Dorn). In order to examine for a niche on the posterior wall a suspension of barium should be given and the patient examined lying on his back.

Akerlund called attention to the fact that diverticula of the stomach may occur independently of ulcer formation, and accordingly describes two kinds of diverticuli of the stomach—the congenital and the acquired. The congenital occurs near the

cardia on the posterior wall and the acquired occurs near the pyloric canal. The congenital is rounded, smooth, mobile, with no infiltration around it and no retraction. It usually shows food residue when the rest of the stomach is empty. The congenital type shows in the erect position a gas bubble in its upper area. One of us on a recent visit to London saw the plates of a diverticulum of the stomach demonstrated by Dr. Arthur C. Hurst, of Guy's Hospital. Kantor, of New York City, recently showed a plate of a congenital diverticulum high up on the pos-



Fig. 129.

terior wall of the stomach. The diverticulum was situated on lesser curvature about 4 cm. below cardiac orifice (Fig. 129).

Friedenwald and Feldman report a characteristic picture of hernia of the cardiac orifice of the stomach through the esophageal orifice. The diagnosis is definitely established by the x-ray with the patient in the recumbent position. The condition is most clearly defined on deep inspiration and straining.

Gray reports a case of diverticulum of the stomach just below the cardio-esophageal orifice which remained filled for a

period of seven days. The finding was purely accidental in the course of a routine examination. The patient had no subjective complaints.

Blaine reports several cases of penetrating ulcer of the greater curvature of the stomach. The author calls attention to the fact that the niche in such a case may be overlooked when the barium enters the small intestine.

To differentiate the niche due to ulcer from that due to an acquired diverticulum, one must take into consideration not only the clinical history but also the indirect evidences that

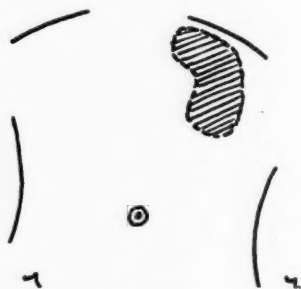


Fig. 130.



Fig. 131.

usually accompany an ulcer and which would be absent in a diverticulum.

Another form of deformity of the stomach caused by an ulcer on the lesser curvature is the snail-form stomach first described by Schmieden (Fig. 130). This form is also known as the tobacco-pouch stomach. Such a stomach is usually situated high in the abdominal cavity to the left of the median line. The pylorus and cardia are so near each other that little is seen of the lesser curvature. The stomach is much smaller than normally. Schmieden attributes this configuration to the excessive contraction of the longitudinal musculature caused by the ulcer. Whereas it is true that in the majority of cases the snail-form stomach is indicative of an ulcer on the lesser curvature, in a number of cases the deformity is not permanent in spite of the presence of ulcer. According to our experience this form

of stomach may also change its appearance and be present only during the stage of active symptoms, and disappear when the subjective symptoms abate. This seems to prove that the deformity is due to functional disturbance of the stomach as a result of the ulcer on the lesser curvature. It must be also remembered that the snail-form stomach may be encountered without any organic changes in the stomach, either due to pressure from without by enlarged pancreas, gas in the transverse colon, or the result of gastric hypertonicity. Therefore, useful as this form of stomach is in the diagnosis and the localization



Fig. 132.

of gastric ulcer, mistakes can often be made if the diagnosis is based on the Roentgen findings alone. Adhesions of lesser curvature to neighboring structures may also produce this picture.

Another direct sign of gastric ulcer situated in the region of the incisura cardiaca was observed by Faulhaber (Fig. 131). The site of the ulcer is indicated by an indentation. This form is very rare.

At times the cascade stomach, first described by Rieder and named cup and spill stomach by Barclay (Fig. 132), may be caused by an ulcer situated high on the lesser curvature.

Faulhaber was the first to have correctly diagnosed an ulcer of the lesser curvature at the site of spasm of the cascade stomach. Since then, however, a great number of other conditions of intra- and extragastric origin have been encountered in the presence of cascade stomach, and, therefore, its value as a sign in localizing gastric ulcer is very limited.

This form of stomach is characterized by a persistent contraction of incisura on the greater curvature just below the cardia, but instead of corpus and pylorus running in the vertical axis, the corpus and pylorus in the cascade stomach adopt the sandal or bull-horn shape. It seems justifiable to assume that such a stomach presents the evidences of regional and partial gastropasm combined (Held and Roemer). The regional spasm is demonstrated by the incisura and the partial spasm by the narrowed, transversely situated corpus and pylorus. This form of stomach is encountered where there is a great deal of gas in the splenic flexure, high position of left diaphragm, and most marked in eventration of left diaphragm. It has also been encountered by Schutze and others in duodenal ulcer. Feissly and Fried observed a case of cascade stomach which was operated and found to be due to the greater omentum being adherent to the anterior abdominal wall. The stomach and duodenum were entirely free from pathology. The gall-bladder was constricted and showed adhesions. A short mesocolon and a very short hepatogastric ligament were found. The authors think that the shape of the stomach was possibly due to the shortness of this ligament and to the adhesions around the gall-bladder. After the operation the patient showed the same symptoms, necessitating another operation. At that time the epiploön was found to be closely adherent to the anterior abdominal wall, the liver, and the surrounding organs. The colon, together with the gastrocolic ligament, was drawn upward and the stomach, therefore, held in an abnormally high position with this ligament. The pyloric end of the stomach was indented by the abnormal insertion of the ligament. A month after the second operation the Roentgen examination again showed the typical cascade stomach. The authors also state that in classi-

fying the various types of this form of stomach distinction should be made first between the true and false cascade stomach. The latter includes those types caused by spasm and air in the colon, which are variable and usually respond to treatment. The true cascade is characterized by permanence of its form and can be caused by pathologic conditions of the stomach, ulcer scars, or by perigastritis, peritonitis, and extraventricular tumors, and also by changes in the normal course of the colon.

The **organic hour-glass contraction** is caused by the formation of connective tissue spreading to the posterior and also to part of the anterior wall of the stomach, thereby dividing the stomach into two compartments. This form of hour-glass is very rare and was very seldom diagnosed correctly before the x-ray era intravital or before operation. The x-ray examination renders the diagnosis very simple. The Roentgen-ray appearance of an organic hour-glass, as illustrated in Figs. 133a, 133b shows the upper or larger compartment of the stomach connecting with the lower or smaller by a canal which indicates the outline of the lesser curvature. In view of the fact that the hour-glass stomach is due to extensive connective-tissue formation of pars media, the canal is not entirely regular in outline. It is, however, very easily differentiated from the hour-glass contraction due to cancer of pars media by the following characteristic features: The upper sac in the organic hour-glass contraction due to ulcer is usually, as stated above, much larger, and when such a case is observed fluoroscopically it is noticed that the food stagnates sometimes for a considerable length of time in the upper sac, and but very little dribbles down to the lower sac along the connecting canal. This is due to the fact that there is always a great deal of associated spasm superadded to the organic changes. In case of ulcer the upper sac usually shows increase in tonus. In the malignant hour-glass contraction the upper sac is smaller than the lower one. The connecting canal is more in the median line and very frequently shows definite manifestations of a defect. If a case of this kind is studied fluoroscopically, the food is not seen to hold at the junction of the upper sac with the canal, but it

drops right down into the lower sac. In addition, the entire stomach is much smaller in size than the organic hour-glass stomach. Another form of organic hour-glass stomach is des-



Fig. 133a.

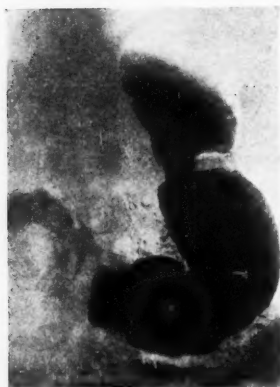


Fig. 133b.

cribed by Le Wald, to whom we are indebted for his permission to insert the accompanying illustration. This form due to gumma gives the stomach the appearance of a dumbbell which is caused

by stenosis of the middle portion of the stomach (Fig. 134). There is apt to be a compensatory dilatation of the esophagus to offset the diminished stomach capacity. The stomach is much smaller than the hour-glass stomach due to ulcer and even smaller than one due to cancer. It may be stated that clinically the organic hour-glass stomach due to ulcer never gives rise to a palpable mass, whereas that due to cancer and especially the one resulting from gumma gives rise to a large palpable mass. If a callous ulcer gives rise to a palpable mass,

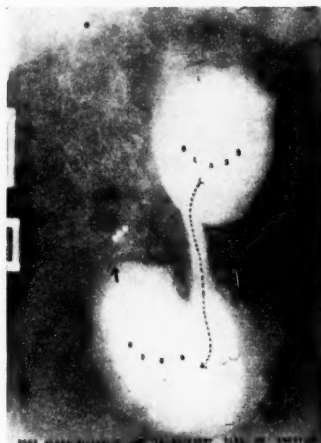


Fig. 134.

it is usually in the left hypochondrium and very tender to palpation. The palpable mass due to carcinoma or syphilis is situated more in the epigastric region or to the right of the median line and is never as tender as that due to ulcer.

ULCER OF LESSER CURVATURE IN WHICH THE ROENTGEN SIGNS ARE ONLY OF TRANSIENT NATURE

The first to be mentioned is the spastic indentation on the greater curvature (Fig. 135) without the presence of a niche on the lesser curvature. It was previously thought that a persistent indentation on the greater curvature is always due to

ulcer on the lesser curvature just opposite the site of the indentation. After, however, a number of such cases had been submitted to operation and no ulcer found, the pendulum swung to the other side and the indentation in the majority of cases was attributed to extragastric conditions. Whereas it is true that it is encountered in a great number of extragastric diseases, as, for instance, chronic appendicitis (Baron and Barsony), duodenal ulcer (Case), cholelithiasis (Carman), if pressure is exercised over the respective affected organs in the course of fluoroscopic examination and also in nervous conditions like



Fig. 135.

vagotonia, it cannot be denied that it is a valuable sign in superficial ulcer of the lesser curvature. The indentation is much more often encountered if the Rieder meal is administered than if the barium buttermilk is partaken of. Of course, this sign is only useful in connection with other clinical symptoms.

A case illustrating its value is quoted: A male patient with a definite clinical history of gastric ulcer presented Roentgen evidences of iliac stasis and ileocecal adhesions, and on repeated examinations spastic indentation on the greater curvature was seen. At the operation John F. Erdman first considered

the pathology in the ileocecal region to be sufficient cause for his gastric complaints. When he palpated the entire stomach no ulcer could be detected. Based on the fact that the indentation was seen on the roentgenogram, the lesser curvature was incised opposite the site of indentation and a small ulcer was found, which was removed. It is quite likely that such small ulcers, if the diseased appendix or gall-bladder are removed, may heal without surgical intervention.

Several observers reported cases of spastic indentation of the greater curvature accompanying syphilis or carcinoma of the stomach. The indentation may also be caused by accumulation of gas in the splenic flexure, but in these cases the indentation is usually broader and the presence of the gas bubble in the colon clears the diagnosis. At times the indentation is only present if the patient is in the recumbent position. In such cases it is most likely due to posture and no pathologic significance should be attributed to it unless all the other clinical symptoms point to ulcer.

The behavior of the peristalsis in ulcer on the lesser curvature is, as a rule, of no aid in the diagnosis. Some authors have reported cases in which the increased tonus in the fornix (fundus) of the stomach, with increased peristalsis in the pars media, were present in ulcer on the lesser curvature. In some cases it has been observed that if there is an ulcer on the lesser curvature with a very large air bag, and excessive secretion, the food does not pass down along the lesser curvature, but drops down in the middle of the stomach. If the secretions are aspirated, the food again passes along the lesser curvature. This sign, however, cannot be made use of in ulcer on the lesser curvature because it is present whenever the cardia is filled with gas and secretions, irrespective of whatever the cause might be. Excessive secretions in the upper part of the stomach are much more frequent in duodenal ulcer than in ulcer on the lesser curvature, and, therefore, this sign must be entirely disregarded.

MOTILITY DISTURBANCE WITH SIMPLE ULCER ON THE LESSER CURVATURE

It has been already stated above that in cases of callous ulcer on the lesser curvature there are evidences of pyloric insufficiency during the early part of digestion. This is also true in simple ulcer of the lesser curvature, only that, in the former, there is delay in emptying of the stomach on account of associated atony; in the latter the emptying time of the stomach is normal or, if delayed, associated pylorospasm is present.

If a florid ulcer is situated high up near the cardia, cardio-spasm results. The entrance of food into the stomach is hindered and the food accumulates above the cardia, causing the spindle-shaped dilatation of the lower part or of the entire esophagus. A very thin stream of food or no food at all is seen to pass through the spastic cardia.

Recently E. Wolf advocated the taking of roentgenograms with the patient lying on the left side in order to demonstrate ulcers situated high on the lesser curvature. His article is illustrated by confirmed excellent roentgenograms.

Lenk and Eisler called attention to the fact that in simple ulcer on the lesser curvature one can, by visualizing the course of the rugæ in the region of the ulcer, arrive at a diagnosis. Normally the rugæ run parallel. In case of ulcer the rugæ converge toward the ulcer. It is best demonstrated by careful fluoroscopic examination and by compression of that part of the stomach by means of the Holzkneckt spoon.

The diagnostic importance of sensitive pressure point on the lesser curvature was first called attention to by Jonas. It is of significance in florid ulcer of the lesser curvature providing the sensitive pressure point is movable with the mobility of the stomach. The sensitive pressure point is much more often present in penetrating ulcer and in perigastritis.

Carman¹ points out important technical aids in the roentgenologic demonstration of lesions high in the stomach and on the posterior wall. He advises: First, that observation of the contrast meal be made as it enters the stomach during gastric

¹ Carman, Russel D., January, 1925, vol. iv, p. 33-39.

filling. Second, careful inspection of the sulci between the rugæ. Third, palpatory maneuvers to approximate the anterior and posterior wall in order to demonstrate small central filling defect or niche or elicit abnormalities on the cardia. Fourth, examination in the Trendelenburg position. Fifth, roentgenography in the oblique and transverse view. In observing the stomach as it fills it is important to watch the first few morsels of food closely. Normally, the meal travels from the esophagus through the upper part of the stomach in a direct course, usually forming a triangle in the cardia with apex down and then gradually descends.

In case of tumor high on the posterior wall the stream of food is deflected to one side or divided. The crater of the ulcer or deeply ulcerating cancer commonly fills. If the pylorus is obstructed and the stomach contains much secretion, the barium column falls through the secretion in blobs which follow no constant paths.

In order to visualize the grooves and rugæ of the gastric mucosa a barium suspension is given. Just below the air-bag, down to the pylorus, grooves running parallel can be seen, usually about ten in number. Transverse grooves may be noted, but are quite short. In case of spastic or organic hour-glass stomach convergent folds are observed. In the region of a tumor or crater these sulci may be absent.

In order to bring anterior and posterior walls together a thin meal should be given. A tumor high on the posterior wall may be demonstrated as a translucent tumor in the gastric silhouette corresponding in size and shape to the growth. The excavation of the ulcer appears as a dense spot usually circular. In the oblique position a projecting niche may be disclosed. Examination in the Trendelenburg position will show a small tumor or ulcer when other positions fail.

ULCER IN THE PARS PYLORICA AND PYLORUS

The direct signs of ulcer in the pars pylorica in the form of niche is very difficult to demonstrate. It may sometimes be possible to demonstrate it if roentgenograms are taken with

the patient lying on the right side. That it is not absolutely inaccessible to Roentgen diagnosis was already demonstrated by Haudek, Schinz, and others who showed a niche in this location. Recently Herrnheiser contributed a most important study regarding Roentgen diagnosis in prepyloric and pyloric regions. His work is based on the study of 40 cases, 19 of which were controlled by operation. In 17 the diagnosis was verified, in 2 the local deformities to be described below, which were attributed to ulcer, were due respectively to chronic appendicitis and pyloric adhesions. The case of pyloric adhesions might have been due to a pyloric ulcer; as there was no resection, positive proof against an ulcer does not exist.

According to Herrnheiser's studies, which we can confirm based on our own experience, the direct x-ray signs in pyloric and prepyloric ulcer are the same as those in the pars media and especially those described by Akerlund in Duodenal Ulcer.

These signs are:

1. Niche.
2. Prepyloric indentation.
3. Retraction.
4. Diverticulum formation.

(1) *Niche*.—Haudek, Schlesinger, Kleiber, Schinz, and others mention the presence of a niche in pyloric and prepyloric regions as a positive sign of ulcer. It is, however, very rarely encountered according to these authors.

The prepyloric niche is situated on the lesser curvature (Fig. 136). Herrnheiser confirms the findings of Lenk and Eisler that the folds of the gastric mucosa in the vicinity of the niche converge toward the ulcer instead of running parallel analogous to ulcer of lesser curvature in the pars media.

The niche of the pylorus proper is seen in the pyloric canal on the lesser curvature (Fig. 137).

(2) *Prepyloric indentation* is usually situated on the greater curvature slightly above the level of the niche. Even in the absence of a niche this may indicate the existence of an ulcer. In the latter event, however, it is of diagnostic significance if it persists on repeated examinations. An indentation of the

lesser curvature in the prepyloric region has no diagnostic significance. Normal peristaltic waves on the lesser curvature in this region being so frequent may simulate niche, and caution should be used to avoid any mistake. Prolonged fluoroscopy will show that the peristaltic wave is changeable in height and location, whereas the niche remains constantly the same.

(3) *Retraction*.—Haudek defines retraction as a condition caused either by stretching or shrinking of the gastric wall brought about by spastic or connective-tissue changes. In the pyloric and prepyloric region retraction may manifest itself (a) as a flattening out on the lesser curvature. The retracted

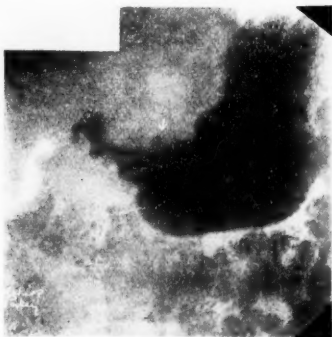


Fig. 136.



Fig. 137.

side shows irregularity, while the non-retracted border is smooth; (b) the retraction may show irregularity on both sides of the pyloric canal causing the canal to be eccentrically situated; (c) the retraction causes a cone-shape appearance of the pylorus simulating carcinoma; (d) elongation of the pyloric canal either the result of spasm of pylorus caused by the ulcer or by scar-tissue formation causing irregularity of the elongated pylorus. Like other signs, the retraction to be diagnostic must be persistent. It must be emphasized that retraction may also be present in duodenal ulcer, cholecystitis with adhesions, or by tumor pressing from without.

(4) *Diverticulum*.—The prepyloric diverticulum is the mirror

image of the bulbous diverticulum in duodenal ulcer, only much more rare. The *ulcus diverticulum* in the pyloric canal proper described by Haudek and later by Schinz is due to a bulging of the intact mucous membrane surrounded by connective tissue. The pouch is usually small, round, sharply outlined, and situated on the greater curvature of the canal.

As a direct x-ray sign of prepyloric ulcer Brugel considered the horizontal prepyloric line (Fig. 138) as a sign of ulcer. This should, however, be utilized with a great deal of caution, as it



Fig. 138.

may be present if there are secretions in the pylorus and in pyloric adhesions. The prepyloric line has been observed by some in cases of duodenal ulcer. It seems to us that the horizontal line merely indicates that the pylorus contains excessive secretions. In view of the fact, however, that recent physiologic studies have demonstrated that the pylorus stimulates the gastric secretions in the fundus, it is reasonable to assume that the excessive secretions in the pylorus is a sign of pyloric stagnation which may be caused by ulcer in the pylorus proper as well as in extragastric lesions. This prepyloric horizontal line

of Brugel is therefore a sign of pyloric dysfunction which may be encountered in prepyloric ulcer, pyloric adhesions, duodenal ulcer, and even functional hypersecretions.

A very important x-ray sign of pyloric ulcer in the florid state is the visualization of spasm of the *sphincter pylori*, characterized by a large pylorus, active antrum peristalsis, and a horizontal line (Fig. 139) marking the termination of the pylorus. The food passes into the duodenum in the form of a very narrow stream. No food may be seen to leave the pylorus for ten to fifteen minutes, even if pressure is exercised on the pylorus

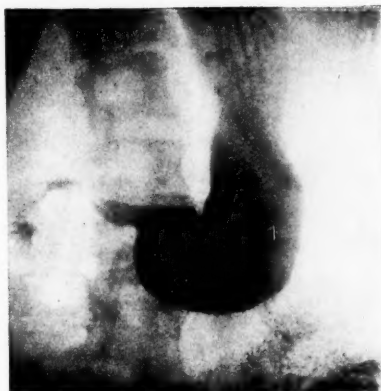


Fig. 139.

while fluoroscoping, or even if pressure is exercised on the lesser curvature in the region of the angularis as advocated by Schutze. The peristaltic hyperactivity of the pylorus may be further evidenced by the teeth-like contractions on the lesser curvature of the pylorus and sometimes similar contractions are seen along the horizontal line. The rest of the stomach may show evidences of atony. Retroperistalsis is never seen in these cases. Motility is moderately disturbed, differing in this respect from organic stenosis due to callous ulcer of the pylorus to be described below. As a rule, the contrast meal leaves the stomach at the end of about six and sometimes eight hours. The stomach also

shows excessive secretions, as indicated by the less dense zone in the pars media and fornix (Fig. 140). Very frequently there are also secretions seen in the pylorus proper. In these cases



Fig. 140.

there are also quite often sensitive pressure points over the pylorus.

ULCER OF PYLORUS

Ulcer of the pylorus proper may occur in the form of erosion of the sphincter pylori which was first described by Julius Schnitzler. It manifests itself roentgenologically by the presence of a very large rounded-out pylorus with active gastric peristalsis and marked delay in the emptying of the stomach, simulating organic pyloric stenosis. The delay is as transient as the rest of the symptoms. The patient may have symptoms lasting for one day, then to disappear for weeks and even for months. Schnitzler states that the symptoms due to erosion of the pyloric sphincter are analogous to the symptoms due to erosion of the sphincter ani. It may at times lead to such high degree of hypertrophy of the pylorus that it may give rise to a palpable mass simulating a tumor, and even on the operating table it may be difficult for the surgeon to decide as to whether he is dealing with a benign or malignant condition of the pylorus, until microscopic examination of the excised pylorus reveals the nature of the disease.

CALLOUS ULCER OF PYLORUS

Callous ulcer of the pylorus is most accessible to Roentgen diagnosis. It is characterized chiefly by dilatation of the stomach and delay in its emptying. The dilatation and the delay in emptying depend on how extensive the callous ulcer is and whether there is associated spasm of the sphincter pylori. In the greatest majority of cases there is always a certain degree of associated spasm which explains the reason why some of the



Fig. 141.

most marked cases may still respond to appropriate medical treatment. By means of Roentgen diagnosis the different stages of stenosis, termed by Boas first, second, and third degree, can be differentiated. In the first degree (Fig. 141) the tone of the stomach is rather increased, as evidenced by the fact that the stomach fills from above downward. The fornix embraces the contents and sometimes it is broader than the pars media and pars pylorica. Peristalsis is very active and its frequency increased. Antrum peristalsis may be so deep as to give the impression that the pylorus is separated from the rest of the stomach. The

enlargement of the stomach is moderate. There is marked delay in the passage of food into the small intestines during the entire course of digestion. One would see, therefore, after the first hour but very little food in the small intestines, and after three or four hours three-quarters of the food may have left the stomach, and the organ is completely empty in ten to twelve hours. This may be explained by the fact that during the very early part of digestion there is marked spasm of sphincter pylori which relaxes a little later and allows a considerable quantity of the food to pass out. In view of the fact that during



Fig. 142.

the first hour of digestion the peristaltic activity of the stomach is so pronounced, atony sets in later in the course of digestion, bringing about marked delay in emptying.

The Roentgen appearance of the second degree of pyloric stenosis may not differ much from the first degree. There is more disturbance in the tone, as indicated by the food dropping down to the lower pole of the stomach and the organ filling from below upward, but after the entire meal is partaken of the entire stomach is filled (Fig. 142). Peristalsis is likewise active, but the evidence of loss of tone manifests itself by the fact that even after three or four hours but very little food has

left the stomach, and the delay in emptying may be from twelve to eighteen hours. In both these forms there is excessive secretions in the fornix, often a large air-bag, and if force is exercised on the pylorus by means of palpation, some food can be forced into the duodenum. In both forms there are also evidences of spasm of sphincter pylori.

The third degree of pyloric stenosis manifests itself by the well known boat-shaped or half-moon-shaped stomach (Fig. 143). During this stage there is often some retroperistalsis.

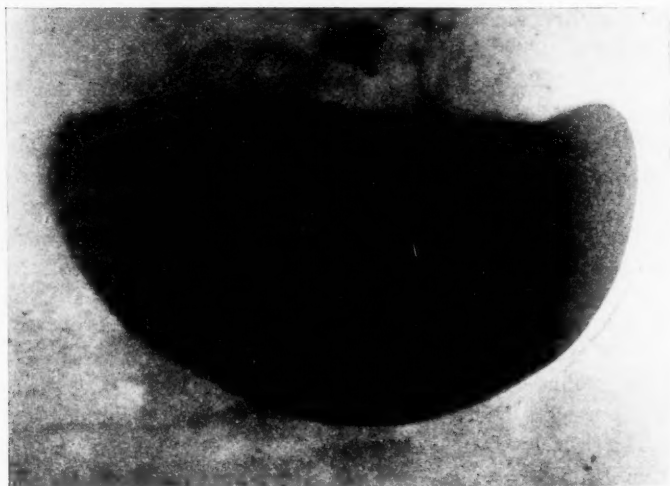


Fig. 143.

No food can be forced into the duodenum by the palpating hand. Such a stomach is never empty and the mobility is likewise disturbed in the greatest majority of cases. The Roentgen manifestations of the third stage of pyloric stenosis may also be present in pyloric stenosis due to carcinoma and sometimes in stenosing duodenal ulcer with extreme atony of the stomach. In the last two conditions, however, the passage of food into the small intestines during the early stage of digestion is not delayed because of the absence of spasm of the sphincter pylori

and one can always succeed in squeezing food from the pylorus into the duodenum with ease if it does not pass out spontaneously. The delay in the emptying of the stomach and the appearance of the stomach are therefore entirely due to associated atony and not so much to the stenosis. The delay in emptying of the stomach justifies the assumption of an intrinsic disease such as stenosing conditions of the pylorus. These are usually ulcer and more rarely stenosing duodenal ulcer. Carcinoma of the pylorus usually stops in front of sphincter pylori and obstruction by malignant growth is generally due to the massive size of the growth, obliterating the lumen and not infiltrating the sphincter. Carcinoma does infiltrate the sphincter pylori, but it is usually associated with an open pylorus, as is found in carcinoma of the rectum where there is an open sphincter ani, and in carcinoma of the lower part of the esophagus the cardia is wide open. This explains why in the greatest number of cases of carcinoma of pylorus the worm-eaten appearance is on the greater or lesser curvature and the pylorus is pivot shaped. The food passes through the pivot-shaped canal like water passing through a hydrant. The emptying of the stomach is rather hastened and if delayed it is due to associated atony of the gastric musculature. There are a number of extragastric conditions which may cause delay in emptying of the stomach simulating pyloric stenosing ulcer.

Every case examined during the acute stage of an abdominal colic secondary to gall-stone attacks, gastric crisis, vagotonia, renal colic, ovarian trouble, will show, if examined roentgenologically at this time, associated pylorospasm which may simulate pyloric obstruction. Migraine attacks at time of examination will also cause delay in emptying of the stomach. The very rare disease, gastrosuccorhea (Reichman's disease) may allow food to pass out, but some barium held in suspension may give one an erroneous impression of pyloric obstruction. Mistaken diagnosis can be avoided by re-examination when subjective complaints are absent and correct data recorded.

If the patient is examined when the small intestines are filled with food, we will physiologically have delay in emptying

of the stomach because of the absence of the hunger of the small intestines (Pawlow). Pathologic causes bringing about delay in the small intestines (adhesions, ileocecal pathology, etc.) will also cause delay in gastric emptying even though pylorus and duodenum are normal. Colonic stasis of functional or organic origin will also cause marked delay in the emptying of the stomach. Pressure of pylorus from without—enlarged liver, enlarged glands, adhesions between pylorus and gall-bladder, tumor of the pancreas or the so-called Harris band (from second part of the duodenum to the parietal peritoneum) causes delay in emptying of the stomach.

Cases of marked ptosis with pyloroptosis and associated duodenal ptosis (the ligament of Treitz being in a fixed position), atony of the stomach due to wasting disease, congenital asthenia, will all contribute to the factors causing gastric stasis. Moderate delay in emptying is a frequent accompaniment of gall-bladder disease. The fact that a stomach may empty itself of a barium meal in normal time and normal progress does not exclude the possibility of intrinsic gastric disease or pyloric ulcer. Clinically, macroscopically, and microscopically residues are encountered in the morning on a fasting stomach.

DUODENAL ULCER

The x-ray diagnosis of ulcer of the duodenum has been greatly advanced by the serial radiography of L. J. Cole. It may be stated that even early ulcer of the duodenum is more readily accessible to x-ray diagnosis than that of the stomach. Roentgenologically, one can even, during the early stages, arrive at the diagnosis of a lesion in the duodenum more readily than one can in the stomach.

For the visualization of the duodenum fluoroscopically we believe that it is best to wait until the duodenum fills spontaneously. If this fails to do so after a reasonable length of time (three to six minutes), it is then advisable to exercise normal pressure on the lesser curvature in the region of the angularis, as advocated by Schutze. Early palpatory intervention on the part of the examiner may lead to contraction of the abdominal

muscles and thus interfere with the proper filling of the duodenum. In the fish-hook type of stomach the first portion of the duodenum can, as a rule, be visualized without any difficulty. In the extreme fish-hook type the duodenum is often seen to the left side of the spinal column. In the bull-horn type of stomach it is sometimes impossible to visualize the first portion of the duodenum despite examination in various positions. In this type, if the first portion of the duodenum is visualized, it forms the most dependent part, and is small, circular, very often the size of a small hazelnut. In some cases the duodenum cannot be visualized until the patient is turned as much to the right as possible so that the first portion of the duodenum is not overlapped by the spinal column. Not infrequently one must resort to a barium suspension which leaves the stomach sooner than the buttermilk meal. The suspension does fill the first portion of the duodenum. In rare cases the patient may have to lie on the right side for fifteen to twenty minutes before the duodenum fills. In our routine method of examination one hour after the meal to see the distribution in the small intestines the entire duodenum may be visualized. In marked spasm of the pylorus and the sphincter large doses of tincture of belladonna, as advocated by Carman, 15 to 20 drops three times a day for twenty-four to forty-eight hours, or 1/120 gr. atropin twice a day by hypo. for twenty-four hours, or papavarin, 1/5 gr., and atropin, 1/120 gr., three times a day, for three or four doses, may be given.

Before going on to a discussion of the Roentgen manifestations of ulcer it may be best to mention the various appearances that a normal pars superior duodeni may have as well as some of the anomalies.

The form and position of the pars superior duodeni may vary in size according to the size and position of the stomach. Like the stomach, the first portion of the duodenum is influenced by the general habitus of the individual and, accordingly, it may be divided into four types:

1. Normal habitus in whom the fish-hook stomach is encountered where the first portion of the duodenum is cylindrical, pear, or pyramidal shaped, often resembling a bishop's cap,

sometimes triangular with the base downward. It is named by Cole the cap, and by Holzknecht, bulbus. Its length is about $1\frac{1}{2}$ to 2 inches.

2. The second form belongs to the stomach, which is moderately hypertonic. In these cases the first portion of the duodenum is somewhat shorter and is directed toward the right and has the shape of a chestnut.

3. The third form is present in the bull-horn-shaped stomach. It is usually visualized with great difficulty in the erect position and is round and small like a hazelnut. In the prone position it is often seen to lie just below the end of the pylorus.

4. The fourth form is seen in the hypo. and atonic stomach. In these cases the first portion is cylindric and considerably elongated.

Both the mobility and motility of the first portion of the duodenum vary in these different forms. In the hypertonic stomach the first portion of the duodenum has restricted mobility, but increased motility. The reverse is the case in the hypo- and atonic stomach. Ordinarily the first portion is the most mobile of the entire duodenum. The third portion runs horizontally from the vertical portion toward the spine, then curves upward, the latter segment being sometimes described as the fourth portion. The suspensory ligament of Treitz marks its termination and the beginning of the jejunum. The duodenum below the bulb is more or less fixed. In the second portion Kerckring's folds are usually seen; the third portion shows clearly the valvulae conniventes.

Anomalies of the duodenum not due to pathologic changes do occur. It is essential to be familiar with these in order not to mistake them for disease. A very long stomach in the status asthenicus type often shows an elongated, cylindric-shaped duodenum.

J. Freud mentions the following anomalies of the duodenum:

1. A cylindrically dilated duodenum or a duodenum the shape of a small, rounded apple may be present without any intrinsic disease. Such a dilated duodenum may simulate dilatation above stenosis. The fact that there is no reflux into the

stomach and the absence of active peristalsis indicates the presence of an anomaly.

2. Of much greater importance are the anomalies where a diverticulum is seen or where the duodenum forms a bow-knot.

The congenital diverticulum of the descending portion is situated usually on the concave side in the midregion (Fig. 144) and has often been encountered at the autopsy table. Since the x-ray era it can be detected in the living. Fluoroscopically one can see peristalsis in the diverticulum. One may even find the stomach empty and the diverticulum still filled with the con-



Fig. 144.—Congenital diverticulum.



Fig. 145.—Bow and knot type of duodenum.

trast substance. Seldom has this diverticulum any clinical significance.

3. The bow and knot type of duodenum has the appearance of a completely closed ring (Fig. 145). The contrast substance usually stagnates in the lower part of the ring. The ring empties itself by strong contraction. This form of descending duodenum often causes delay in the emptying of the stomach. A short bow-knot of the descending duodenum may be sometimes of transient nature and be caused by pressure of the distended ascending colon.

4. Occasionally part of the descending duodenum may be so elongated that the lowermost point reaches the crest of the ileum.

Reichman reported a case of multiple diverticula, diagnosed roentgenologically.

ROENTGEN MANIFESTATIONS IN DUODENAL ULCER

The direct signs mentioned in the order of importance rather than of frequency are the following:

1. *Niche*.—As early as 1911 Freud in Holzkmnecht's laboratory observed a niche on the lesser curvature of the duodenum which he correctly interpreted as being due to ulcer. Soon after Haudek observed a case. In analogy to gastric ulcer one finds on the lesser curvature of the first portion of the duodenum a niche in a penetrating ulcer of the duodenum. This important α -ray sign was forcibly brought to our attention and its diagnostic importance firmly established by the elaborate work of Akerlund in the clinic of Forssell. Akerlund showed that, just as in the stomach, the lesser curvature of the duodenum being practically a continuation of the lesser curvature of the stomach, the ulcer is most commonly situated in that part of the duodenum extending to the posterior wall. He also showed that this part is very frequently the seat of a niche. On the greater curvature of the duodenum as on that of the stomach, opposite and slightly above, there is an indentation. This finding was at first met with contradiction. At present, however, Haudek, Schintz, and others are firmly convinced that the findings of Akerlund are absolutely correct. It is understood that the niche must be persistent and source of error may sometimes be found in a parabolbar fleck of contrast, lodged in Kerckring's folds. At times a contraction on the lesser curvature of the first portion of the duodenum, causing temporary bulging, may also simulate a niche. It is, however, important to remember that a real niche is almost invariably accompanied by spasm of the greater curvature opposite the seat of the ulcer. Akerlund correctly states that the niche may be caused by lack of substance in the wall resulting from ulceration and not necessarily be due to penetration.

Akerlund correctly emphasizes that the niche need not necessarily be the result of penetration. As a rule, it is the callous or the indurated ulcer in the wall of the duodenum proper that causes the niche. This varies in size from the smallest pinhead to half a walnut shell. It is mostly rounded and may some-

times contain a bubble of air in the top. The basal or the pyloric surface of the bulb is very seldom the seat of a niche. In many cases there is a segmentary contraction in the ulcer plane on the greater curvature opposite the seat of the niche caused in part by a longitudinal tightening of the retraction of the bulbar contour in the neighborhood of the niche. This bulbar deformity constitutes a miniature of a well-known ulcer deformity of the stomach. The segmentary contraction is often very broad in relation to the height of the bulb. It at times comprises a large portion of the entire bulbar shadow. Both niche and retraction are often proportionately larger in ulcer of the first portion of the duodenum than in that of the stomach, and they occur more frequently. Akerlund found it in 60 per cent. of the cases. This was confirmed recently by Joseph S. Diamond, and we can state that it is so, based on our experience. The retraction may occasionally be caused by the ulcer, and sometimes by infiltration and edema of the mucous membrane in the vicinity of the ulcer. If the retraction affects the basal portion of the bulb the central bulbar recess becomes obliterated on the lesser curvature, giving the impression that the lumen of the pylorus is eccentrically situated. This may explain the pyloric insufficiency.

A niche on the greater curvature of the duodenum was only observed once by Akerlund. George and Leonard quote a case where the niche was on the greater curvature of the bulb which resulted in effacing the Cole defect. The pyloric lumen was eccentrically situated toward the greater curvature. The spasticity in both these cases was on the lesser curvature. The type of niche just described is, according to Akerlund, termed the "profile niche"; in contradistinction to this, he described the "enface niche," which is not seen from a profile, but over the entire surface of the anterior and posterior walls. He observed 5 such cases. Such a niche is circular or oval, corresponding to the dimension of the surface of the crater of the bulb.

The reason why the niche is seen mostly on the lesser curvature, although the ulcer on the operating table or at autopsy proves to be on the posterior or anterior wall, has been explained

by De Quervain as follows: This apparent anomaly as to the situation of the niche is due to the fact that the ulcer being situated nearer to the lesser curvature, be its seat on the posterior or anterior wall, it becomes adherent to the posterior abdominal wall or liver, and so the part of the stomach or duodenum which is the seat of the ulcer forms a fixed point, replacing the anatomic fixed point formed by the gastrohepatic ligament. The ligament is thus stretched and the stomach or duodenum, depending as to whether the ulcer is on the anterior or posterior wall, is pulled either anteriorly or posteriorly, and the lesser curvature is brought more to the front. This, therefore, makes the lesser curvature the most prominent part and makes the niche appear as if it were on the lesser curvature, although it is, in reality, on the posterior or anterior wall, depending on the seat of the ulcer. This explanation, however, holds good only in cases where adhesions are found, but there are cases of niche on the lesser curvature of the stomach or duodenum without adhesions, and, therefore, this explanation does not hold good in these cases. Akerlund explains this phenomenon on the basis of the arrangement of the longitudinal musculature of the stomach and duodenum. On account of this ligamentous and muscular arrangement, the lesser curvature remains more or less fixed. Because of the spastic condition of the bulb, which accompanies duodenal ulcer, the duodenal wall is drawn over to the lesser curvature by the spasm in the circular muscles. It is on account of the deep spasm of the circular muscles that the niche, with the rest of the duodenal wall, is drawn together and appears to be on the lesser curvature. The reason why the niche is found on the postmortem or operating table in the location where the ulcer actually lies is because the duodenum or the stomach, the seat of the niche, is then empty, whereas during the Roentgen examination the organ is filled, the lumen more or less cylindric, and therefore the niche is visible on the lesser curvature.

Diamond states that the niche may sometimes be effaced by spasticity of the first portion of the duodenum. He gives belladonna according to the method of Carman, for two or

three days, to relax the spasm, and then re-examines. When the bulb is relaxed he states that the niche again becomes visualized. This does not correspond to our experience, as shown in the accompanying figure (Fig. 146).

In this polygram the niche was evident during the spasm and was effaced a few minutes later when the duodenum was filled.

This illustration is inserted because it concerns a case that was recently operated upon by Dr. William Linder, at the Israel Zion Hospital, Brooklyn. The patient had symptoms of a duodenal ulcer for a number of years. The duodenum was

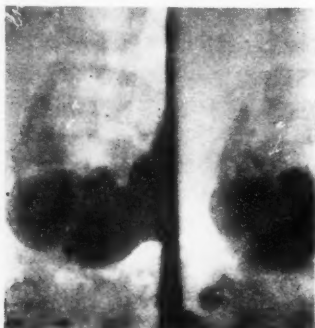


Fig. 146.

normal in outline when completely filled. The niche was seen only when the duodenum was spastically contracted. We were doubtful in our diagnosis. The clinical symptoms were those of ulcer and the patient was put to bed and given an ulcer diet. During the first week of observation the ulcer perforated and necessitated immediate operation. A perforated ulcer of the duodenum was found.

Since then a number of other cases have been seen where the niche was best observed during the stage of spasm and was entirely effaced when the first portion of the duodenum filled out completely.

V. C. Knapp reports findings similar to ours.

It appears logical to us that a niche should be better visualized when the first portion of the duodenum is not filled to its full capacity, but when it is more or less in a state of spasm. The niche is really not on the lesser curvature, but more on the posterior wall and, therefore, complete filling may efface it.

2. *Cole Defect*.—L. G. Cole was the first to call attention to the importance of the deformity of the duodenal contour in duodenal ulcer. This defect manifests itself as a local contraction or narrowing in the bulbar shadow. Next to the niche it is of greatest importance in the diagnosis of duodenal ulcer. The defect in the duodenum may manifest itself in the form of



Fig. 147.



Fig. 148.

a general distortion of the entire duodenum, giving the bulb the appearance of a miniature pine tree or a bit of branched coral, or there may only be a deformity at the base. Sometimes only a small indentation is seen on the lesser or greater curvature. The deformity may also be that of the clover-leaf form (Fig. 147). The deformed cap shows its contraction on the side of the ulcer. The proximal part of the cap on the side opposite the ulcer is often dilated, simulating a diverticulum (Fig. 148). In a deformed cap the pyloric lumen leading from the sphincter to the duodenum is usually eccentrically situated. In case the deformity is not only present on both sides of the cap, but involves the entire cap, the appearance

of a pivot-like bulb is seen. The entire filling of the bulb may cause it to become worm shaped. At times the deformity is marked by a retraction of the proximal part of the duodenum, especially of its inner half, brought about by the failure of the ulcerated part to fill (Fig. 149). This gives the impression that the gap between pyloric sphincter and the first portion of the duodenum is very wide. In reality, it is due to the fact that the ulcerated area does not hold the contents, analogous to a tuberculous ulcer in the cecum. This, too, was first

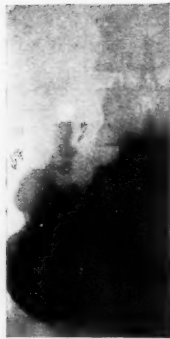


Fig. 149.



Fig. 150.

pointed out by Forssell, recently confirmed by Haudek. In connection with deformity, spastic duodenum may be mentioned. This is not absolutely pathognomonic of ulcer, as it is often encountered in cases where the first portion of the duodenum does not fill out completely because of spasm of the sphincter pylori. If spasm persists and is present on repeated examinations in connection with a very marked dilated pylorus, it can be utilized as a sign of duodenal ulcer. This corresponds to the observation made by Finsterer, who rightly called our attention to the fact that in many cases of duodenal ulcer the

pylorus is often seen on the operating table to be hypertrophic and dilated. Another deformity is "hour-glass duodenum" (Schlesinger), and, if persistent, is likewise a valuable positive direct sign (Fig. 150).

3. *Bulbous Pouch or Diverticulum* (Fig. 151).—The bulbar defect may be of functional nature or the result of spasm. It may occur on the pyloric, medial, and lateral contour. It is most often present on the lateral contour of the greater curvature. It varies in depth and may sometimes, during different



Fig. 151.

examinations, be broader and narrower and often disappear. If it affects the basal bulbar area or the top of the bulb it may be easily overlooked. Such defects are not very common on the pyloric surface. If present, it is very small, size of a pea at most, and sharply defined. It is due to local contractions of the muscularis mucosa, possibly the result of a fissural ulcer on the duodenal side of the pyloric sphincter. Such a defect may precede the niche on the lesser curvature by many months. The spastic bulbar contraction is more marked during the later stage of digestion. Akerlund explains the paradoxical retention

of Haudek due to this spastic contraction, which increases with digestion.

On account of the retraction of the ulcerated area, due to scar formation, pouch-like dilatation forms above the area of retraction. The late pathologist, Hart, observed this in a great number of his postmortem cases. These are not true diverticuli, although they are often interpreted as such. In the pathologic material shown to us by Ceelen we became convinced of the frequency of such pseudodiverticuli, the result of the retracted ulcer. They are often found below and on the upper side of the cap, thereby causing the cap to become asymmetric. Such pseudodiverticuli may contain contrast substance after the rest of the duodenum has emptied itself. It is not rare to find an ulcer niche with a pseudodiverticulum. A pseudodiverticulum may appear as being directly connected with the cap, or as parabolbar fleck, or as multiple small flecks in which case it is impossible to determine to what part of the duodenum they belong. Pseudodiverticuli may also appear in the form of spur-like projections. The contour of a pseudodiverticulum is irregular, as a rule, in contradistinction to a true diverticulum, which is very rare and regular in outline.

4. *Bulbar retraction* is the deformity which consists of a tightening in the longitudinal direction of the contour of the bulb which thereby loses its normal curvature and becomes shortened, giving the bulb an asymmetric shape. It is analogous to the snail form of the lesser curvature of the stomach due to ulcer. It is always localized on the lesser curvature. It may be purely spastic, but very often it is produced by cicatricial tissue in the wall of the duodenum.

5. *Localized pressure point* over the cap is likewise an important objective direct sign of duodenal ulcer provided the pressure point moves with the mobility of the duodenum and tenderness is elicited without too deep pressure.

6. *Dilatation of the cap* (Fig. 152) as a direct sign of ulcer must be utilized with great caution. In rare cases where the ulcer is situated at the junction of the first and second portions of the duodenum, leading to incomplete stenosis, marked dilata-

tion of the first portion of the duodenum may be present. As a sign, however, that the duodenal dilatation is due to a stenosing ulcer, the dilatation must be persistent, and marked contraction of the duodenum and retroperistalsis must be present. Dilatation of the first portion of the duodenum, if transient, has no diagnostic significance at all, but even if persistent without other signs of duodenal stenosis, it is often present in ptosis of the fish-hook type of stomach, and also in diseases of the ileocecal region, especially chronic appendicitis and ileocecal valve incompetency.

7. *Phthisis bulbi* (Fig. 153) indicates the non-filling of the entire cap, whereas the descending portion fills. It is also con-

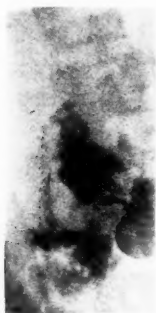


Fig. 152.



Fig. 153.

sidered a direct sign if present during repeated examinations, and if the clinical history justifies the suspicion of duodenal ulcer. Sometimes the ulcer in the duodenum manifests itself by the contrast substance adherent to a small part of the duodenum in the form of a coin (Holzknecht).

INDIRECT SIGNS

The indirect x-ray signs of duodenal ulcer in order of diagnostic importance are:

1. *Hyperperistalsis*.—This is mentioned first because it is present in a much greater number of cases than hypertonicity.

Barclay in London was the first to call attention to this important sign, and it has so impressed itself on us that we value it almost as much as the deformity of the cap. Hyperperistalsis sets in early and is so active and the contractions are so deep that the stomach seems divided into three or four compartments. The duration of each peristaltic contraction is much longer than normal and the intervals between contractions are much shorter.

2. *Hypertonicity* is present also in a certain number of cases.

3. *Dextroposition of pylorus and duodenum*.

4. *Pyloric insufficiency*.

5. *Rapid emptying of the stomach* during the early part of digestion and a small six-hour residue in the stomach (paradoxical residue—Haudek).

6. *Hypermotility* of the small intestines and also hypermotility of the proximal colon.

7. *Hypersecretion* is shown as a layer of fluid less dense than the rest of the contrast (Schlesinger).

8. *Gastropasm*.—Duodenal ulcer is generally associated with some spastic manifestations of the stomach. It is sometimes in the form of an incisura or an hour-glass contraction. This may be large and deep or very superficial. It may occur anywhere along the greater curvature. It is sometimes brought out, as shown by Baron and Barsony, by pressure on the duodenum.

9. *Teeth-like Contractions*.—Schutz called attention to the fact that teeth-like contractions on the greater curvature are often encountered in duodenal ulcer. These teeth-like contractions are due to the contrast depositing in the folds of the mucosa along the greater curvature and are encountered in a number of intra-abdominal functional and pathologic conditions, but may also be found in duodenal ulcer.

10. *"Cascade" Stomach*.—The "cascade" type of stomach, or as termed by Barclay, the "cup and spill" stomach, which we believe to be due to regional spasm, is also at times encountered in duodenal ulcer, but is, by no means, to be considered an important sign of duodenal ulcer since it is encountered in so many other extragastric conditions.

All these indirect x-ray symptoms may also be present in a number of other intra-abdominal diseases, and may, on the other hand, be absent in duodenal ulcer. As stated above, however, to discount the value entirely of these indirect symptoms and only to diagnose duodenal ulcer on the basis of deformity of the first portion of the duodenum would mean missing the diagnosis altogether in a certain number of cases.

It is well known that postmortem examination and also from the observation of the surgeon that many an ulcer may be so superficial as not to cause deformity of the duodenum. The scar does not extend beyond the mucosa. In such cases a defect or some definite deformity cannot be expected roentgenologically.

The pathologic statistics of Perry and Shaw, and in a great number of cases that we saw in Erdheim's and Ceelen's pathologic laboratory, prove how carefully one must examine the interior of the duodenum in certain cases in order to locate a superficial scar or an open ulcer. The surgical statistics such as those of Mayo confirm this. Rovsing showed that in 41 out of 110 cases of duodenal ulcer he would have missed the ulcer entirely if he had not opened the duodenum or if he had failed to examine it by means of gastroduodenoscopy. Akerlund states that he repeatedly looked in vain on the serosa of the duodenum for small ulcers, where clinically he had a right to expect them, and missed them until the duodenum was incised. He even quotes a postmortem case where an ulcer of 3 x 3 mm. was only discovered after cutting open the first portion of the duodenum. In such small ulcers it is clear that direct visualization can hardly be expected, and they can give only the indirect x-ray symptoms. It is important to remember, however, that indirect x-ray signs are only obtainable during the stage when the patient has symptoms. This is to a certain extent also true of some of the direct signs unless the deformity is due to extensive scar formation. It has been our observation that in cases where the deformity of the duodenum is so marked as to point to the seat of the ulcer, most of the indirect x-ray signs are absent.

Marked delay in the emptying of the stomach, causing considerable six-hour residues, is only present if there is an ad-

vanced stenosing duodenal ulcer. The differentiation as to whether the stenosing ulcer is on the pyloric or on the duodenal side can be judged by the fact that in a stenosing pyloric ulcer no matter how long we observe our case fluoroscopically, either no contrast substance is seen to leave the stomach at all, or but very thin streaks of food can be squeezed out by exerting forcible pressure on the pylorus. In a stenosing duodenal ulcer,



Fig. 154.—Niche on lesser curvature of duodenum with indentation opposite.

on the other hand, pyloric insufficiency is present, so that, during fluoroscopic examination, food is seen to pass out of the stomach in a continuous stream.

Another very important differential sign is the following: That in advanced pyloric stenosis, gastric peristalsis, although active, is usually transient. The stomach is seen to contract for short intervals of time and soon dilates again. The periods of dilatation are much longer than those of contraction. In duo-

denal ulcer, on the other hand, hyperperistalsis continues to be active for minutes and there are only very short intervals of relaxation. In duodenal stenosis, marked contraction of the first portion of the duodenum and retroperistalsis in the duodenum are seen. The fact that sometimes an ulcer may be present in stomach and duodenum at the same time has been emphasized by Mayo, Moynihan, Chaoul, Akerlund, and others. The Roentgen diagnosis in these cases would depend on the direct visualization of both ulcers, as, for instance, a niche in the region of the stomach as well as a deformity of the duodenum.

DIFFERENTIAL DIAGNOSIS

It is self-evident that in a disease where so many x-ray signs have been described the differential diagnosis is quite difficult. This is especially true of the indirect x-ray symptoms. Many intra-abdominal diseases of a functional or organic nature may give rise to an x-ray symptom-complex closely resembling that of duodenal ulcer.

1. *Gall-bladder Disease.*—In diseases of the gall-bladder there is often hyperperistalsis, hypermotility, and transverse position of the stomach. There is very seldom, however, hypermotility of the colon, and paradoxical residue is much rarer in gall-bladder disease than it is even in duodenal ulcer. The sensitive pressure point, fluoroscopically observed, is limited in gall-bladder disease to the gall-bladder and not to the duodenum.

2. *Chronic appendicitis* may also give rise to hyperperistalsis, but there is never, as a rule, pyloric insufficiency and never hypermotility of the small intestines; in fact, there is delay in ileum which may be due to spasm of the ileocecal sphincter, or, as stated by Hurst, failure of relaxation of the sphincter.

3. *Functional diseases of the stomach*, with stigmata in the vegetative nervous system, especially vagotonia with gastric symptoms, give rise to hyperperistalsis and transverse position of the stomach, but there is never pyloric insufficiency, and if there is a delay in the emptying of the stomach, it is usually transient and the residue much larger than it is in duodenal ulcer. There is no colonic hypermotility, but rather evidence of

spasticity of the colon. Of course, the diseases named may be associated with duodenal ulcer, and one must always, therefore, be very guarded in ruling out an ulcer, even if one of the above-named diseases is present. In fact, chronic appendicitis and gall-bladder disease are very frequently associated with ulcer of the duodenum and, as correctly pointed out by Moynihan, Deaver, Mayo, and others, probably often precede duodenal ulcer. This is also true, as shown by von Bergmann, Westphal, Katsch, and others, of cases where there is unbalance in the vegetative nervous system.

The differential diagnosis between pyloric and duodenal ulcer by means of Roentgen examination is not always very simple. In general, it may be said that in pyloric ulcer gastric motility is much more disturbed than it is in duodenal ulcer. Pyloric insufficiency is never present. There is a greater tendency to pylorospasm, and especially spasm of the sphincter pylori. Hypermotility of the small intestines and hypermotility of the colon are likewise very rarely present in pyloric ulcer. In cases where we have no direct evidence of duodenal ulcer and only the indirect signs, such as increased peristalsis and pyloric insufficiency, the rapid emptying may cause the pylorus to appear narrow and so simulate a pyloric scirrhus carcinoma. Careful fluoroscopy and repeated examination, and, if necessary, also taking a few roentgenograms will safeguard against such a mistake. In achylia gastrica we also at times encounter an open pylorus, but in these cases there is usually no hyperperistalsis.

Even in cases where the first portion of the duodenum does show deformity, the differential diagnosis as to whether it is due to ulcer or adhesions as a result of extraduodenal disease is at times very difficult.

From the standpoint of differential diagnosis, we must consider the following:

Periduodenal adhesions may cause irregularity of the duodenum, having its origin not in duodenal ulcer, but generally in the gall-bladder, sometimes pylorus, and at times, even the colon. Sometimes periduodenal adhesions are encountered secondary to chronic appendicitis or even diseases of the right

kidney. In these cases there is irregularity of the contour of the duodenum, especially confined to the upper part of the first portion of the duodenum. There is also, as pointed out by Lorenz, frequently a small air-bubble in the upper part of the duodenum at its junction with the descending part. The filling of the bulb may be persistent and the duodenum is to the right of the median line, often showing restricted mobility. Extensive adhesions around the duodenum may cause the constriction of the first part of the duodenum at its junction with the descending part so as to give rise to duodenal stenosis. The characteristics of such stenosis, as pointed out by Holzknacht, are: Marked dilatation of the first part of the duodenum; sometimes visible peristalsis in the first portion of the duodenum; the descending portion of the duodenum fills slowly, and, after it is filled, it may also show retention leading to dilatation and even antiperistalsis. The lower the seat of stenosis is in the duodenum, the more active is the peristalsis above the seat of stenosis. Holzknacht termed this phenomenon "peristalsis without any effect." It has already been pointed out that advanced duodenal stenosis leads to gastric retention, simulating strongly pyloric stenosis, and can only be differentiated roentgenologically by the fact that in duodenal stenosis the emptying of the pylorus into the duodenum is not interfered with and, therefore, the duodenum fills readily, whereas in pyloric stenosis the duodenum fills with great difficulty.

Duodenal stenosis is often the result of adhesions between the gall-bladder and the duodenum. Adhesions of the first portion of the duodenum may sometimes cause distortion of the entire duodenum, especially marked on the greater curvature, where pouch-like projections are seen. The fact that such projections are present on the greater curvature of the duodenum and not on the lesser curvature speaks for adhesions rather than ulcer, because the pouch-like projection due to ulcer is much more common on the lesser curvature than it is on the greater curvature.

Stenosis due to adhesions between the gall-bladder and the duodenum may occur in any one of the three portions of the duodenum. If it occurs in the first portion it is characterized by the fact that the portion of the duodenum below the seat of

the stenosis is markedly dilated, the pylorus is almost always insufficient, the suprastenotic portion appears as an uninterrupted continuation of the pyloric canal (Bier, "Duodenalzapfen"), the dilated portion of the duodenum shows active peristalsis and sometimes often antiperistalsis. In advanced cases the stomach shows marked atony. Stenosis of the descending portion of the duodenum is in the majority of cases caused by adhesions of the duodenum with the gall-bladder, very seldom the result of ulcer of the duodenum. The most frequent seat of the stenosis is in the midpart of the descending portion at a point of the Papilla Vateri. It may also be caused by tumors pressing from without or carcinoma of the head of the pancreas. Enlarged lymphatic glands at the head of the pancreas may sometimes cause it. In these cases the area above the stenosis is persistently filled. The seat of stenosis is marked by a narrow strip of contrast, and the portion below is markedly dilated, showing Kerckring's folds very clearly.

Stenosis in the pars inferior has its seat in the region of the duodenojejunal flexure. In mild cases it manifests itself only by persistent filling of the pars inferior; when more advanced it manifests itself in the form of C-shaped dilatation of all the portions of the duodenum. At times, and especially in cases where the stenosis reaches a high degree, the entire duodenum is so overfilled with duodenal and pancreatic secretions that it may cast a shadow even without the presence of contrast substance. The shadow, however, is naturally not as dense as is the duodenum if it contains contrast substance. Often the layer of secretions is recognized by the formation of a horizontal line at the widest point of the fluid, upon which there is often also an air-bubble. If the stomach is dilated and markedly ptosed, the filled duodenum may be overlapped, especially in the vertical position, because it is covered by the stomach. It is, therefore, always important to examine the cases both in the vertical and horizontal position. It must be emphasized that in order to diagnose stenosis of the third portion of the duodenum, the overfilling of the duodenum must persist during repeated examinations, as transient dilatation of the entire duodenum is often due to gastropptosis.

At times the entire duodenum may fill completely and even be markedly dilated, simulating stenosis in cases of pyloric insufficiency resulting from achylia gastrica or carcinoma of the stomach.

Besides the common causes mentioned for duodenal stenosis one must always remember that transient stenosis may be caused by marked meteorism of the transverse colon. Persistent stenosis may be caused by tumor of the head of the pancreas, cyst of the pancreas, tumor of the right kidney, mesenteric tumor, and retroperitoneal glands. Assmann points out that in tuberculous peritonitis there is often marked distortion of the duodenum caused probably by adhesions and enlarged glands at the duodenojejunal flexure. Bier also calls attention to the fact that transient spasticity of the duodenum may cause temporary duodenal stenosis. Bier and Assmann quote cases of duodenal stenosis, proved by operation, in which the duodenum failed to fill. This is important to remember because, as stated above, pyloric stenosis differs from duodenal stenosis by the fact that in the former case the duodenum does not fill, whereas in the latter it does. Bier, as well as Assmann, explains the failure of the duodenum to fill in their cases by the fact that the duodenum was full to its capacity with pancreatic and duodenal secretions so that no contrast meal could enter the duodenum. It is also very likely that in these cases retroperistalsis was so marked that the stomach refilled quickly with the duodenal contents, giving rise to gastric retention instead of retention in the duodenum. In very rare cases carcinoma of the duodenum may give rise to a C-shaped, overfilled duodenum. Very few cases of this kind are reported in literature. This dilatation is not due to the carcinoma of the duodenum, but to the fact that the tumor spreads to the head of the pancreas, causing stenosis.

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CONTRIBUTION BY DR. BRET RATNER

NEW YORK

TRANSITORY BLINDNESS AFTER CHICKENPOX

VARICELLA is a disease fortunately devoid of complications except in rare instances. The complications, for the most part, are secondary infections of the vesicles and there have been cases reported of the pock directly invading the eyeball. For example, Fuchs reports in his manual the observation of a girl twenty-two years old who, during the decline of the eruption, had abundant precipitations on the inferior-posterior surface of the cornea with opacities of the vitreous body and a large spot of choroiditis. The vitreous body finally became transparent, but a spot of choroid atrophy remained. There are cases reported by Comby of the typical eruption with small ulcerations on the conjunctiva.

Terson¹ reports a case of a girl, eighteen, just convalescing from a benign varicella accompanied, in the right eye, with a corneal lesion which dated back some days. Examination showed a central corneal grayish ulceration the size of a small millet seed, which was not deep, without hypopyon or iritis. There was complete and rapid recovery from the corneal involvement which Terson believed was a case of a ruptured vesicle.

Wyler² reports the case of a girl, five years of age, who had a mild chickenpox. The second day of the eruption the child could not open the right eye, the lid became swollen, and the conjunctiva slightly reddened. The center of the cornea presented a punched-out area, perfectly round, which measured 3 mm. in diameter. The base of this ulcer was deep. The eye was treated with atropin and yellow oxid of mercury. There was no tendency for this to spread and in two weeks the ulcer slowly healed. Wyler believes that this was the eruption of a

pock on the cornea. It is strikingly similar to the case reported by Terson.

There are several other cases reported of the involvement of the eye, but all these appear to have some other complicating factors, such as purpura hæmorrhagica, ring-worm, etc.

Miller and Davidson³ have reviewed the nervous complications of varicella, reporting one of encephalitis. They find a small number of complications, such as convulsions, myelitis, peripheral neuritis, etc., and these are few indeed.

The English writers have written considerably on the relationship of herpes zoster and varicella.

The case I would like to present is one of double optic neuritis in a boy, complicating varicella, producing a state of temporary total blindness with complete return of vision. As will be shown below, this case is of extreme rarity and is reported primarily to emphasize the fact that cases of acute infections in children complicated by sudden blindness should be given a hopeful prognosis, as a return of vision usually ensues.

Case.—On May 15, 1921 I was called in to see a boy, M. L., four and a half years old, who, nine days after a mild varicella, had on that morning suddenly become blind. When I examined the boy I found the scabs of a mild varicella on his body, face, and scalp. He was physically very sturdy and well nourished with a mentality and sensorium that were perfectly normal. His only complaint was his imploring us to help him see and his groping about with outstretched arms. There was no damage to his outer eye. His pupils were widely dilated and immobile. Ophthalmoscopic examination of his eye-grounds showed a marked pallor of his left disk and a marked congestion and swelling of his right disk. The child remained totally blind for the ensuing six days and his eye findings remained unchanged. On May 21st I was hurriedly called to see the child because of his complaining of the light. His pupils, at this examination, for the first time gave a sluggish reaction to light, but none to accommodation. His left disk presented the same pallor, but the right disk seemed less congested. The child's

vision from then on gradually began to return, and ten days later his eyes reacted perfectly to light and accommodation and vision was apparently normal. The last time the boy was seen was on June 6th, two weeks after his vision began to return. Wassermann was negative. Urine analysis was normal. Blood counts were normal. x-Ray of his skull and accessory sinuses were negative. No permission for a lumbar puncture was granted. No medication was used.

Dr. Carl Koller consulted with me on the study of the patient's eyes, and the following is a record of his careful and thorough findings:

May 18, 1921 (third day of blindness).

Left eye: Amaurotic.

Right eye: Shows perception of light (projection of light above and nasally only).

Ophthalmoscopic:

Left eye: Pallor of disk (atrophy?), dilated veins, arteries of normal caliber.

Right eye: Optic neuritis with moderate swelling. Veins very much dilated, arteries normal.

Note.—The left eye apparently had started first and blindness occurred when the right eye also became involved.

May 21, 1921:

Dr. Ratner reports reaction of pupils and return of light vision.

May 23, 1921 (eighth day of blindness):

Pupils narrower, react promptly. Peripheral field of vision of either eye good except in the left eye in the lower nasal quadrant. Seems hypersensitive to light.

June 6, 1921 (twenty-second day):

Sees apparently well. Central vision could not be tested. Peripheral field shows the left eye still slightly defective nasally. Right eye perfect.

Ophthalmoscopic:

Left eye: Extreme pallor as before (not really an atrophy).

Right eye: Swelling almost entirely disappeared. Disk outlines clear.

Note.—No central vision taken because child objected to covering right eye.

REVIEW OF LITERATURE AND DISCUSSION

Chavernac,⁴ in 1908, reported what we believe the first case of optic neuritis following varicella. Although he credits Hutchinson⁵ with reporting the first case in 1886, we find, in studying

Hutchinson's report, a young woman of twenty-eight developed optic neuritis accompanying a secondary syphilitic eruption which was mistaken for varicella, and it seems that Antonelli,⁶ who had previously referred to this case of Hutchinson's as being unique, made a similar error and attributed it to varicella.

Chavernac's Case.—The patient, G. S., a boy of eleven who had contracted varicella on February 5, 1905, after a few days rapidly recovered from his illness without any complications. He recalls, however, that his vision became diminished immediately after he became sick and a fortnight later he could not read and in June, 1905, he could no longer distinguish the number of fingers at a distance of one meter. In November, 1905 the child was seen by Chavernac (that was nine months after his illness). His examination presented a normal sclera and choroid. The papillæ seemed hyperemic; the arteries seemed normal, but the veins were tortuous and dilated. In some places some fine newly formed capillaries were noted. The optic disks were not clear and their diameters increased, the borders were veiled, of undecided contour, and contained several finely punctate hemorrhages. The retina had a normal aspect. The field of vision was retracted about 20 degrees in all diameters. These findings were diagnosed optic neuritis, that Chavernac believed a result of the varicella which had immediately preceded it. The boy had been treated with mercury inunctions throughout the nine months of his blindness. Chavernac discontinued this and gave a series of fifteen subconjunctival injections of 5 to 6 drops every two to three days of sodium cinnamate until a complete cure was affected. The left eye became entirely normal. In the right eye, however, the field of vision was retracted 5 degrees, the papilla a little pale in the center. The vessels had a normal aspect, but the edges, finely fringed, were pigmented almost throughout their entire length. The child was re-examined in April and November, 1906, May, 1907, and January, 1908, the same condition as noted above persisting in the right eye. Chavernac concludes that one should never despair of the return of vision no matter how serious the aspect may seem. He believes that in cases of optic neuritis of infectious origin mercury should

be employed with discretion, as in this case the application was inactive and may have done harm.

Paton's Case.—The only other case that I could find in the literature was that reported by Paton⁷ in 1918. The patient, R. J., male, aged fourteen, had had varicella at the same time his two brothers did in December. The attack was a severe one, with a temperature of 103° F. and some headache. On the third day the patient found that his left eye was blind and sight has remained defective in that eye ever since, that is, four months later. On April 9th the vision of the right eye was normal and the left was diminished. The right pupil was active, but the left pupil did not maintain the contraction well when the right eye was shaded and sometimes showed a condition resembling hippus, but more irregular. The right optic disk was normal. The left optic disk was pale with the edges blurred, especially in the upper half, but no swelling. Retina somewhat obscured, but showing some irregular spottings toward the macula. Visual field showed an irregular central scotoma and some peripheral limitation. Rhinoscopy and x-ray examination of accessory sinuses were negative.

In 1884 Nettleship,⁸ Gay⁹ in 1893, Stephenson¹⁰ in 1902, and Moore and his collaborators¹¹ in 1922, discuss a condition in infancy which Sydney Stephenson called "fleeting amaurosis." This condition affects infants usually under two years of age. There is a history of sudden illness, associated with fits, head retraction, and vomiting. Immediately following upon this the child no longer appears to see. This failure of sight may be of short duration and clears up soon after the general illness has subsided. In some cases with a similar onset no recovery of sight ensues and though these latter cases cannot rightfully be classified under "fleeting amaurosis," the underlying pathologic process would seem the same. In the case in which no recovery of the sight occurs atrophy of the optic disk is usually present, whereas in the case of true temporary amaurosis no fundus abnormality is to be seen. It has been suggested that the pathologic basis of these cases of true temporary amaurosis consists of a basal meningitis which seals the foramen of Majendie

and so causes a distention of the third ventricle. This distention produces pressure upon the optic chiasma. In those cases in which the amaurosis is temporary it is suggested that the sealing of the foramen of Majendie is of short duration. Whereas, in those of permanent blindness the closure of the foramen is of a long enough period to do permanent damage to the chiasma, due to prolonged pressure.

Barrett¹² in 1920 reported a case of this "fleeting amaurosis" in a girl nine years of age, which followed two weeks after an attack of influenza. At that time she complained that she could not see the blackboard, lifted her eyelids with great difficulty, and had considerable pain in her head and eyes. Her pupils were dilated and inactive, but the fundus and media were absolutely normal. Barrett regards this case as remarkable, as the child was nine years old, and corresponds to the type of acute cerebral amaurosis seen in infancy, first described by Nettleship and further studied by Gay, Stephenson, and Moore.

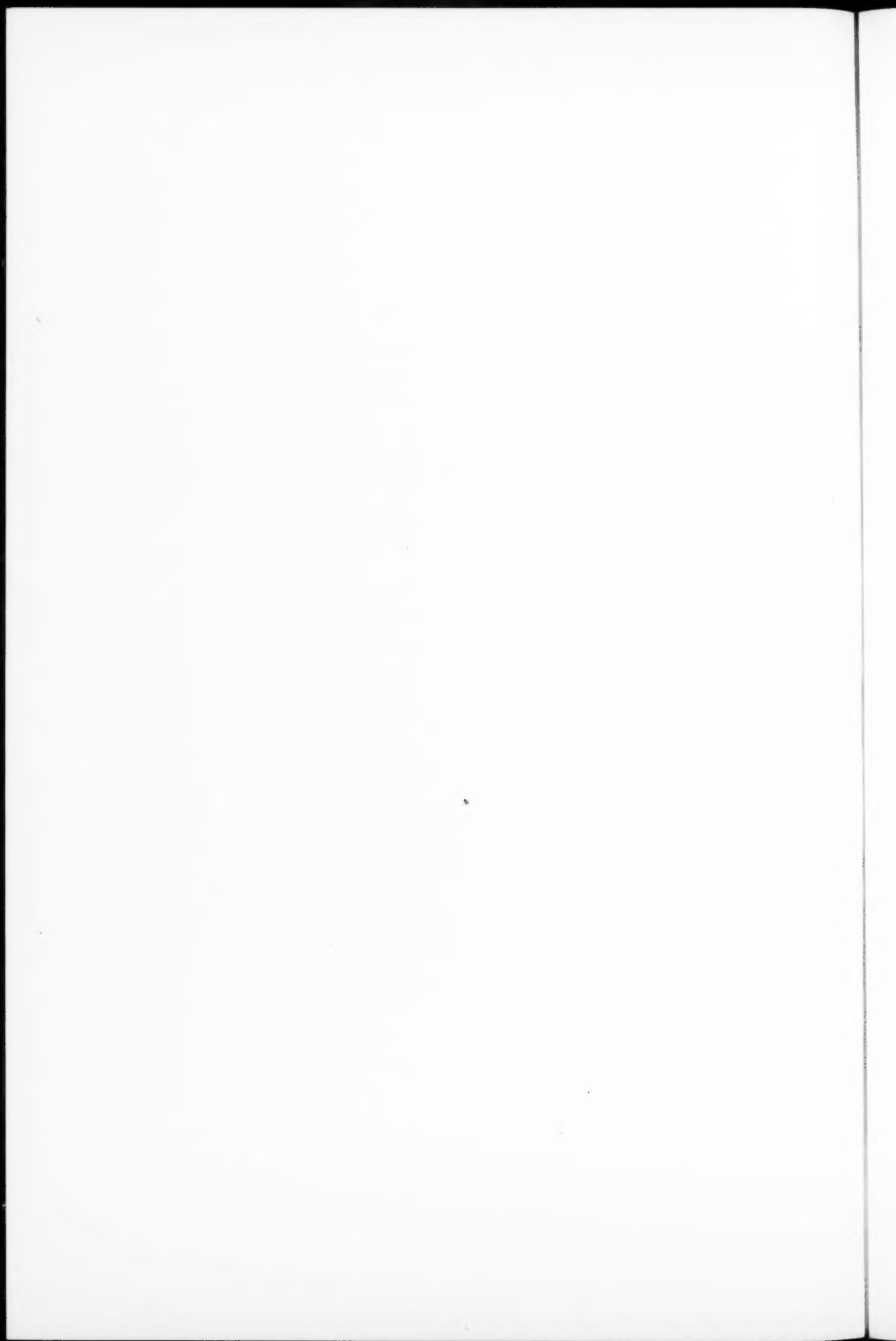
In conclusion, we feel justified in presenting our case as one of double optic neuritis following varicella, because of the supportive evidence given by the only two other cases we could find in the literature, namely, those of Chavernac and Paton. Furthermore, there are other cases reported of optic neuritis following such diseases as scarlatina, variola, etc.

It would appear, from this discussion, that temporary blindness in children following acute infections should be divided into two large groups. On the one hand, those due to pressure from a blocking off of the foramen of Majendie and, on the other hand, those due to direct retrobulbar neuritis of toxic origin, to the latter of which our case belongs. The prognosis in either instance appears to be hopeful. The cases apparently have no relation to the severity of the disease and, although the vision returns, some pathologic condition of the optic nerve may persist.

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ECZEMA IN INFANCY DUE TO PROTEIN SENSITIZATION

THE cause and the treatment of infantile eczema has been a perplexing problem and a review of the literature bids fair to leave one even more uncertain. It is not our purpose in this clinic to discuss all the causative factors and treatments that have been advocated by many able investigators, but only to present evidence bearing directly on protein sensitization as the causal factor.

Case I (F. I.).—The mother of this infant states that at about three months of age the face, which had previously been rather dry, developed a raw, oozing, vesicular type of eczema which was very itchy. The eczema continued on the face up to six months of age and the infant developed a bilateral cervical adenitis. This was at the time regarded as due to absorption from the marked eczema. Up to ten months of age the eczema was localized to the face, but had become a very severe type. At thirteen months, when I first saw her, the eczema was extremely marked, crusted, oozing, bleeding; involving the entire face, neck, scalp (hair destroyed), also both arms, legs, and body. There was marked adenitis of the neck and mild adenitis of the inguinal and axillary regions. The child was sent to the wards of New York Nursery and Child's Hospital. Her arms and legs were restrained in order to prevent scratching and all eczematous parts were anointed with a 3 per cent. euresol in Lassar's paste (without salicylic acid). She was put on a regular one-year diet. The following day the child was tested out to all the proteins that might have been in her diet and environment and was found to be sensitive to egg-white. The diet was immediately ordered changed by the elimination of all egg-containing foods. The tests were done, October 27, 1921. Hospital note by intern stated that the eczema had improved remarkably in the past

week since egg had been omitted from the diet. On November 2, 1921 the intern noted evidence of a little eczema on the forehead which was not severe. The body, extremities, and face were clear.

Referring to the previous history of this child, we find that when she was seven and a half months old she was given a half an egg-yolk every day, and at eight and a half months the child received a whole egg. When we first saw her she was on a diet consisting of an egg a day, Dryco, and cereal in the form of cream of wheat, farina, and zwieback.

On November 5th we discovered that the child was getting zwieback which contains egg. This was eliminated from the diet. From then on the child made rapid progress, and on November 19th was discharged from the hospital. The child was last seen on February 20, 1922, and the eczema was entirely gone. Attempts were made to desensitize the child by subcutaneous injections of egg-white. This was kept up for a short time and the child was then lost sight of.

Discussion.—In this case it was definitely a question of the taking of egg which caused the eczema. The child was observed by us for four months. For the latter three months the only thing done for the child was the elimination of egg from the diet, and the eczema cleared up and did not return. She had previously been unsuccessfully treated for a period of ten months.

The indication here is that in a severe and refractory type of eczema we had found the cause to be the ingestion of egg-white, the elimination of which effected excellent results. The eventual cure would depend entirely upon the elimination of egg-white and desensitization.

Case II (V. D.).—Girl, age thirteen and a half years. Referred by Dr. William Goldstein. This child had an early infantile eczema which cleared, but recurred at six months of age and has persisted on and off up to the present. When I first saw this patient on December 30, 1923, the *eczema* was present on the bends of the elbows, the bends of the knees, and both

ankles. It was of the oozing, itching, bleeding type, and was not present at all times, but had periods of remission and exacerbation. The child was found to be sensitive to garlic and pyrethrum. It should be noted at this point that this child's parents are European Indians and their meats and vegetables are usually eaten spiced, garlic being a very common element in their dietary. It should be noted further that the father stated that even at the age of six months the child was given a taste of home-made spiced lamb which is made with spices and garlic.

In addition to local treatment, we ordered the complete elimination of garlic from the diet, and we forbade use of pyrethrum-containing roach powders in the home.

The child was last seen on April 2, 1922, and reported only moderate improvement of her condition. However, during the course of treatment the child was asked to keep a strict diary of her food intake, and on February 12th we find a note that she had indulged in bologna (containing garlic), and we can therefore infer that there have been other infringements.

Discussion.—This case demonstrates that although we did find a specific causative factor in an eczema of long duration we were unable to effect a most probable cure because of the unwillingness of the patient to co-operate with us. Our purpose in citing this case is to show that one of the reasons that protein sensitization fails in its efficacy is that the finding of the incriminating substance is only part of the story and where we are confronted with changing the racial dietary habits of an entire family we are beset with a grave difficulty, and we may therefore fail in the cure, even though we may be correct in diagnosis.

Case III (D. M.).—The following case will be gone into at great length in order to bring out the many phases that enter into it, this case having been studied from the inception of the eczema and thence over a period of two and a half years.

Referred by Dr. Ten Eyke Elmendorf. At the age of five weeks the mother noticed a moderate crusting on the infant's

forehead and head—the rest of the face absolutely clear. This condition gradually spread to the face and progressively became worse and spread down to the arms and legs, and became crusted, itching, and bleeding in type.

April 12, 1923: The child was first brought to me on this date at the age of four and a half months, and presented a very severe and very itchy, crusted eczema involving the entire face and head, much of the body, the arms and legs, generalized enlargement of the glands, and an abscess at the back of the neck. She gave a positive allergic reaction to egg-white. General local treatment for the care of the skin was given, the use of water interdicted. Inasmuch as the infant was on the breast, eggs in every form were eliminated from the mother's diet.

April 20th: The child markedly improved. Weight, 11 pounds, 2 ounces. Eczema of head and body very much diminished. Knees and cheeks still very bad. Child less restless—sleeps better. Allergic tests positive for milk and egg-white. Suggestive for beef, chicken, and casein. Further general directions were given; besides eliminating egg, the mother was to take all milk boiled.

May 4th: Weight, 12 pounds, 1 ounce, a gain of 15 ounces in two weeks. Tests repeated gave the same reaction as above. Directions given to continue as above, also to try bathing the child in bran bath with bicarbonate of soda, providing it agreed with her.

June 1st: Age six and a half months. Weight, 13 pounds, $12\frac{1}{2}$ ounces, a gain of $27\frac{1}{2}$ ounces in past twenty-eight days. Child's entire body cleared, with the exception of slight roughening of the face and sides of the head and the hands. At this time the suggestive reaction to casein was positive. Child was started on an evaporated milk formula, to be given instead of one breast feeding. One week later farina was started. In addition, 1 drop of raw milk in a teaspoonful of warm water just before a breast feeding once a day was ordered. Furthermore, a change from a three- to a four-hour feeding schedule was instituted.

July 6th: Age seven months, nine days. Weight, 14 pounds,

4 ounces, a gain of $7\frac{1}{2}$ ounces in past thirty-six days. Takes cereal well, and generally takes about 6 ounces of the bottle. Moderate amount of dry eczema on left ankle and back of both arms. Slight roughening of both cheeks—a few papules on head. Since four-hour schedule was adopted, the child did not gain well. Mother's breast secretion markedly diminished. Child had been bathed in bran and bicarbonate, and the mother noticed that the skin was more sensitive after it. Gradual weaning was instituted, finally putting the child entirely on evaporated milk formula with barley-water as diluent. Orange juice was started, and cereal advised twice a day. The raw milk was gradually increased to 3 drops a day. General directions for care of skin continued, and further emphasized need for prevention of scratching by restraining arms. Resume bran baths.

July 20th: Weight, 13 pounds, 7 ounces, a loss of 13 ounces. Further tests showed positive reaction to wheat. Advised discontinuance of farina on account of this positive reaction to wheat. Use cream of rice instead of farina. Formula increased. Continue giving the raw milk, but reduce to 2 drops.

August 3d: Age, eight months and one week. Weight, 13 pounds, $14\frac{1}{2}$ ounces, a gain of $7\frac{1}{2}$ ounces in two weeks. Further tests: Positive reaction to beef, chicken, lamb, and barley. The child has a slight roughening of the face with marked improvement since the removal of the wheat. The child has begun to gain again. Directions: Discontinue barley on account of positive reaction, and use plain boiled water as diluent. Carrots to be started.

August 10th: Weight, 14 pounds, $1\frac{1}{2}$ ounces, a gain of 3 ounces. Body absolutely clear. Has a few papules on the scalp. Diagnosis of early rickets. Tests: Negative reaction to potatoes, carrots, and oats. Directions: Start oatmeal. Continue 2 drops of raw milk a day. Add 2 ounces of boiled milk to the water in which the rice is cooked.

August 17th: Slight roughening of the face. Child is happy and content. Directions: Discontinue bran baths (wheat sensitization). Start potatoes. Increase boiled milk in cereal to 3 ounces.

August 25th: Weight, 15 pounds, $2\frac{1}{2}$ ounces, a gain of 7 ounces. Slight roughness of both cheeks and both legs—head and body both excellent. Directions: Continue as above. Start cod-liver oil.

September 1st: Weight, 15 pounds, 12 ounces, a gain of $10\frac{1}{2}$ ounces in seven days. Face slightly rough.

September 7th: Nine months old. Weight, 16 pounds, 3 ounces, a gain of 7 ounces in six days. Further tests: Pea and bean negative. Directions: Start 1 drop of beef-juice once a day. Give 2 drops of raw milk three times a day. Start thirty-minute hard-boiled egg-yolk. Start peas and string beans and spinach.

(It should be stated that in the carefully worked out and complete directions given the patient, orders were given to start only one new food at a time, in a minute quantity, increases made gradually, and new additions made slowly, so that we might trace effect of each new food.)

September 13th: Weight, 16 pounds, 7 ounces, a gain of 4 ounces. Further tests: Silk positive; spinach and corn negative; tomato positive. Still very slight dry eczema on cheeks and legs. Directions: Discontinue raw milk, beef juice, and egg-yolk for two weeks. Start cornmeal and hominy as cereals.

September 28th: Age ten months. Weight, 17 pounds, $3\frac{1}{4}$ ounces, a gain of $12\frac{1}{4}$ ounces in sixteen days. Eczema entirely cleared, apparently on account of the elimination of the above substances. Directions: Start cauliflower, lettuce, celery, and asparagus. Resume raw milk and work up gradually to 6 drops a day.

October 6th: Weight, 17 pounds, $13\frac{1}{4}$ ounces, a gain of 10 ounces in one week. Child has mild roughening of both cheeks. This has developed since the milk was resumed; however, advised continuing milk.

October 19th: Weight, 18 pounds, 7 ounces. It is interesting to note here that today the child's arms presented definite eczema. This seemed to be due to the fact that the child wore a new silk and wool shirt (the silk test having been positive, as

noted on September 13th). As wool test was negative, advised return to plain wool shirts.

November 3d: Weight, 19 pounds, a gain of 9 ounces. Condition of arms apparently due to silk. The arms have practically cleared up since the silk was eliminated. Possibly the slight roughness on the face is due to silk ribbon on cap. Directions: Start 1 drop of 1 : 100 dilution of raw egg-white a day.

November 17th: Weight, 19 pounds, 4 ounces, a gain of 4 ounces in two weeks. Eczema entirely cleared.

December 1st: Age, one year. Weight, 19 pounds, 9½ ounces. The child is below the average in weight for her age, but she is shorter than the average, and weight is good for height. She is 28 inches tall and the average weight for this height is 18 pounds, 13 ounces. She has six teeth. Skin is absolutely clear except for a slight roughness of the face. Directions: Continue 1 drop of 1 : 100 dilution of egg-white. Work up raw milk to 8 drops. Start apple sauce, baked apple, and stewed prunes.

December 29th: Weight, 20 pounds, 8 ounces. Slight dry eczema on cheeks. Directions: Start bread, thrice baked.

February 8, 1924: Age fourteen months. Interesting note: Child has a few spots of eczema on arms and back—very slight. While examining the child, noted a hive on the chest and thought it was due to the silk of my secretary's waist or the mother's. To prove this, the child's back was rubbed against Miss S.'s silk shirt waist, and in a few minutes the entire back was covered with hives. Absorbent cotton, when rubbed on the chest, did not produce the same result.

We do not think it necessary to continue detailed accounts of visits through the second year, for from February 8, 1924 to September 1, 1925 the child has progressed well, with practically no eczema except for occasional mild exacerbations, which were shown to be due to sensitization to cauliflower, carrot, potato, turnip, oat, and pork.

As the child was found to be sensitive to these various foods, they were eliminated from her diet. At various intervals, however, the mother was advised to try these offending foods, very thoroughly cooked, and in very small portions. When given in

this manner, they were well tolerated. However, the child has throughout this period taken average amounts of thoroughly cooked milk, beef broth, beef, chicken broth, chicken, lamb broth, lamb, and whole egg. The child also partakes of stale toasted bread, and occasionally small amounts of egg-containing cakes. She continues to get a few drops of raw milk, and 1 to 2 drops of raw egg-white a day, and occasionally a few drops of fresh beef-juice. Additional new foods required by a child of this age, including fish, fruits, etc., have been added gradually, to none of which D. M. is sensitive.

The child is seen once in six months and on the last visit, September 1, 1925, after nearly two and a half years of observation she weighed 31 pounds. Height, 35 inches. She is slightly over weight and taller than the average child of her age. She has a well-balanced diet, and has developed normally. The mother still wears silks, and the only eczematoid condition that the child has is a slight roughening on the hands, giving them a chapped appearance.

Discussion of Case III.—This infant was brought to us and was carefully studied. She was found to be sensitive to the proteins of milk, egg-white, wheat, barley, oat, potato, tomato, beef, chicken, pork, carrot, turnip, and silk. As soon as these offending proteins were ascertained, they were eliminated and substituted by other foods to which she was not sensitive and which answered the child's requirements (for example, a rice cereal for wheat cereal). Or where, as in the case of milk, no other food could be substituted, a denaturized form of the food was given. Nothing else in the way of treatment was instituted except in the beginning, when local treatment was used.

It will be noted from the details of the case that though we did treat the case scientifically, at no time was the child's physical well-being sacrificed, though we were handicapped in being confronted by sensitization to practically all of the common foods. The child now takes the offending proteins in small amounts, and has a well-balanced diet. We are attempting in a gradual way by feeding small amounts to build up an immunity against the various harmful proteins. Whether she will even-

tually be entirely cured of her protein sensitivity, is a matter for the future. For the present, we have cleared her condition by specific means, namely, the elimination of offending proteins and a gradual building up of tolerance.

This detailed report seems to us to emphasize the importance of a complete and thorough study of such cases, and the need for absolute co-operation from the patient. Of course, in dealing with protein sensitization in infants and children, one must never lose sight of their nutritional requirements. For without the understanding of the nutritional side, only partial good can be obtained. To treat these severe infantile eczema cases, there must be an appreciation of the various problems in hand, and a meticulous plan of procedure maintained.

SUMMARY

We have presented here 3 cases of severe eczema which have been shown to be caused by protein sensitivity, and we have further shown that the elimination of offending proteins has effected good results. Many more cases just as carefully worked up could be presented, but there would be needless repetition of parallel types which these 3 cases exemplify.

That there may be a goodly number of eczema cases which do not respond to protein sensitization investigation and do respond to the various methods of treatment advocated by others, we will grant; such cases, however, do not, as a rule, belong to the severe refractory type that we have presented above, but rather are of the milder facial and other local types. We will also agree that there are spontaneous cures. When cases, however, resist local and general treatment, they should be studied from the standpoint of protein sensitization; in fact, they should only be undertaken after they have been observed for a number of weeks, and do resist such treatment. Furthermore, they should not be taken on unless a most complete study can be made.

Our detailed reports seem to us to emphasize the importance of a complete and thorough study of such cases, and the need for absolute co-operation from the patient. We feel very strongly that if all cases were as carefully studied and followed

there would be fewer failures. Of course, such investigation entails much time and trouble to the patient, but we believe that we have shown that certain good results may be accomplished, and the co-operation of the patient thereby gained. In dealing with protein sensitization in infants and children, one must never lose sight of their nutritional requirements, for without the understanding of the nutritional side only partial good can be accomplished.

PULMONARY TUBERCULOSIS IN EARLY INFANCY SIMULATING BRONCHIAL ASTHMA

Case I.—J. W., male, white. On October 29, 1919 a child was discharged from the New York Nursery and Child's Hospital, nine weeks of age, weighing 5 pounds, 5 ounces, typically marantic, with a negative Von Pirquet. At a second visit to the hospital, January 28, 1920, the child was five months old, and at this time presented no lung condition, had a negative Von Pirquet, and showed the general signs of marked malnutrition.

The third admission to the hospital was on December 1, 1920. The child was fifteen months of age and had been referred to the wards. There was a history of the child having had a "cold" for the past month. He had been gaining very poorly, and there was a history of the father having tuberculosis.

January 12, 1920: Admission note: Pale, undernourished, with temperature of 101° F., weight 12 pounds, 5 ounces. There were fine subcrepitant râles heard throughout both lungs. Posteriorly, in the left suprascapular area there was definite bronchial breathing and bronchophony of the crying voice, with large moist râles. Throughout both bases fine subcrepitant râles were heard, more pronounced on the left side. There was a generalized adenopathy. A diagnosis was made at this time of pulmonary tuberculosis and rickets. x-Ray examination showed marked hilus, right side, congestion and peribronchial thickening, enlarged bilateral hilus glands between right upper and middle lobes, some suspicious stippling suggestive of tuberculosis. x-Ray diagnosis: Acute bronchopneumonia with suggestive tuberculous changes in region of right hilus (Fig. 155).

January 13th: Von Pirquet strongly positive.

January 14th: General condition the same. The left upper posterior part still presents bronchial breathing and the re-

mainder of the chest is almost clear, with an occasional râle over the right base.

January 15th: Afebrile, losing weight. Occasional dry râles heard over the left base, bronchial breathing with occasional moist râles present. In the right lower axillary anterior line there are a few sonorous râles.

January 16th: Afebrile. Left intrascapular region shows bronchial breathing, remaining lung clear.



Fig. 155.—Case I: J. W., January 12, 1920.

January 18th: Marked pallor. Signs unchanged.

January 20th: Received a transfusion of 100 c.c. of maternal citrated blood.

January 21st: Color improved since transfusion. Chest signs clearing. Few dry râles. Over hilus bronchovesicular breathing, no râles.

January 26th: For the last five days, few signs in the chest. Another citrated blood transfusion of 115 c.c. given.

January 28th: Right chest posteriorly suprascapular breathing. Below the inferior angle of the scapula, on the right side, fine râles heard. Expiratory grunt and moderate substernal retraction. Slight cyanosis of finger-tips and definite clubbing of fingers.

January 31st: Dulness and bronchial breathing over the right suprascapular, intrascapular, and axillary regions. Resonance over the base also impaired and some fine râles. Cyanosis and clubbing still present, spleen moderately enlarged.

February 1st: α -Ray examination, diffuse shadow occupies entire right chest through which pulmonary markings may barely be determined. Left lung shows considerable peribronchial thickening and congestion. Diagnosis: Fluid right thoracic cavity.

February 2d: Marked dulness below the inferior angle of the scapula on the right side. Thoracentesis in this region produced no fluid.

February 8th: Temperature had mild course. Respiration labored. Right side still presents flatness, bronchial breathing, and a few râles. A second thoracentesis negative.

February 11th: Respiration still labored. Dulness and bronchial breathing still present on right side, no râles. Clubbing of finger-tips increasing. Transfusion, 100 c.c. citrated blood. Immediately following transfusion, child developed marked dyspnea and beginning cyanosis. Examination of chest revealed typical asthmatic breathing. Adrenalin subcutaneous injection gave immediate, but only temporary, relief.

February 14th: Dyspnea (similar to that after transfusion) still present. Signs in chest typically asthmatic, wheezing being present except for moderate tubular breathing in the right upper posterior.

February 17th: General condition poor, patient propped up in bed, marked dyspnea, with no cyanosis. Characteristic expiratory wheezing, asthmatic in type. Diffuse moist râles heard over both lungs with sibilant râles on expiration. No bronchial or bronchovesicular breathing.

February 19th: Marked dyspnea, slight cyanosis; asthmatic

breathing, very pronounced. Submucous râles spread diffusely throughout both lungs.

February 22d: General condition very poor, breathing labored, asthmatic in type, signs in chest showing little or no change except for an apparently increased solidification of the right upper lobe. No enlargement of the mesenteric glands noted.

March 1st: General condition poor, patient propped up in bed, breathing laboriously. No cyanosis. Both lungs have asthmatic type of breathing and no definite area of consolidation.

March 4th: Condition still poor. Marked dyspnea and cyanosis. Left purulent otitis media, asthmatic breathing very marked. Von Pirquet strongly positive.

March 5th: Asthmatic breathing and dyspnea continuing, cyanosis more marked; 4 P. M., child ceased breathing.

Autopsy.—March 6, 1921, 3 P. M. (Dr. B. S. Denzer), No. 738. Male child, eighteen months old.

General: Body that of a moderately emaciated male, white child, 66 cm. long, depression of left ribs, simulating one-sided Harrison's groove. No skin lesions. No general gland enlargement. Anterior fontanel 3 by 2 cm. No craniotabes. Muscles: Yellowish and attenuated.

Peritoneal cavity: Abdomen markedly distended, about 25 c.c. yellowish, slightly turbid fluid being found. No tubercles on parietal peritoneum, but the fringe of omentum showed a number of hard, slightly grayish nodules.

Pericardial sac: Excess fluid 20 c.c. clear, straw colored.

Pleura: *Left*, practically obliterated by adhesions. *Right*, completely obliterated by very fine adhesions such as are observed in adults, necessitating tearing of lung and stripping it from chest. Lung could not be separated from diaphragm. Chest and wall presented ragged appearance, studded on account of innumerable tubercles. In some places the pleura was thick and studded on account of tubercles. Mediastinum: Part of right side a mass of edematous jelly-like material with the various structures matted together on account of granulated tissue, evidently tubercular. Thymus degenerated, pale white, group of

thick strands difficult to distinguish from the edematous mediastinal tissue.

Heart: Opened *in situ*. No congenital anomaly. The heart is displaced to the left so that the right border is about the mid-line and the left border is at the anterior axillary line (apex). Valves normal. Heart pale.

Lungs: *Right*, interlobar fissures obliterated. There are several processes:

1. There is a scattering of grayish tubercles, particularly at apex.
2. Diffuse chronic passive congestion, dull deep salmon color.
3. Fibrosis finger-like connective tissue processes extending into the lung, particularly at the base.
4. Caseation, two or three areas about 5 mm. in diameter in the lower lobe, composed of cheesy material.
5. A few patches of raised grayish-red areas on account of bronchopneumonia in the central portion of the lung in the grayish red stage.

Left: 1. At apex, a fringe of emphysema surrounding a central raised reddish gray area.

2. Scattered tubercles.

3. Lower part of upper and all of lower lobe on section showing a pinkish-gray appearance, each lobule standing out clearly above surface.

Bronchi, trachea, and glands: Trachea normal. Bronchi slightly injected. The right paratracheal glands are very large, measuring 2.5 cm. in length, caseous on section. The gland at the bifurcation of the bronchi is large, caseous, and adherent. There is a slight, but definite narrowing of the right bronchus probably due to pressure of the glands. One bronchial gland a considerable distance from the right lobe was caseous.

Liver: 3860 gm. Presents numerous surface tubercles. Cloudy swelling, fatty degeneration. On section presented tubercles in parenchyma.

Spleen: 240 gm. Surface rough, presenting tubercles. On section, cloudy swelling and tubercles.

Kidneys: 600 gm., capsule smooth, strips easily; few suspicious tubercles.

Pancreas: 180 gm. Negative.

Adrenals: Postmortem changes.

Intestines: Several processes: 1. Jejunum, tortuous; varicose veins.

2. Ileum, ulcers 3 to 4 mm. in diameter.

3. Showers of grayish tubercles in ileum.

Glands: Mesenteric, hard, not caseous, moderately enlarged.

Paravertebral, shotty, several near cardia and stomach caseous.

Brain: Negative, intracranial sinuses negative.

Bones: Section of costochondral junction shows normal straight line.

Diagnosis: Marked malnutrition, pulmonary and generalized miliary tuberculosis. Tuberculosis of bronchial and tracheal glands.

Discussion and Summary of Case I.—At nine weeks of age and at five months of age, respectively, the infant was observed in the hospital and gave all the evidences of being a typical case of malnutrition. At both of these periods he gave a negative Von Pirquet reaction and showed no lung condition.

At fifteen months of age he again came under observation, entering the hospital markedly underweight and with a history of an acute respiratory infection and definite evidence of having been exposed to tuberculosis through the father. While under observation the character of the lung signs, *i. e.*, their variability from day to day, pointed to a diagnosis of tuberculosis. The Von Pirquet was found to be positive, and the child being a little over one year of age we regarded this as indicating an active state of pulmonary tuberculosis. The x-ray diagnosis pointed to a suggestive tuberculosis. The child continued on the downward path, gradually developing moderate cyanosis and clubbing of the fingers, becoming emaciated. The temperature was always of a low-grade variety.

Two transfusions were given one week apart, and three weeks later a third transfusion was given. Immediately following the

third transfusion the child developed what appeared to be a definite attack of asthma, which was temporarily relieved by an injection of adrenalin. However, from then on until the child's exitus, twenty-four days later, the asthmatic breathing was continuous day in and day out, with only slight remissions. Throughout this period there were, however, definite signs of dulness on the right side which made us think that we were dealing with fluid, but we could obtain no positive results after thoracentesis. Various râles were also heard throughout this period.

Because of the synchronous occurrence of the asthmatic breathing with the third transfusion, we were led to believe that there might have been some relationship between the injected blood and the production of the asthma, but in so far as the asthmatic breathing continued unremittingly from this point until the end, we felt that the effects of the transfusion were purely coincidental and that the previous signs of cyanosis, clubbing of fingers, etc., were all early indications of the final bronchial obstruction which ushered in the asthmatic breathing.

The autopsy findings recorded above indicate very strongly that the enlargement of the tuberculous calcified tracheo-bronchial lymph-nodes, producing a definite narrowing of the bronchial tree, had a great deal to do with this infant's asthmatic breathing, and that the signs of consolidation and râles were still further evidences of a more diffuse tuberculous pathology.

Case II.—L. J., male, colored, one year old. Admitted to the Children's Wards of the City Hospital, January 31, 1923.

On admission the child appeared to have some marked obstruction to breathing. The breath sounds were noisy and rapid, accompanied by an expiratory grunt. The *ali nasi* were dilating excessively. The pharynx and buccal membranes were normal. Tonsillar nodes were not enlarged. The cervical glands were moderately enlarged. There was marked glandular enlargement of the left inguinal region. The chest was typically rachitic, presenting a Harrison groove. There was generalized aden-

opathy. The abdomen was distended, giving a tympanitic percussion note. The liver and spleen were moderately palpable.

Examination of the chest revealed symmetric percussion resonance impaired at the left apex and down to the fourth rib on the right side. The breath sounds were harsh, the expiratory phase being moderately prolonged. At various places musical (sibilant and sonorous) râles could be heard. Inconstant crepitant râles were heard over the left and right apex. There was a suggestive pleural friction-rib audible in the left axilla and near the left apex. The temperature was of low-grade variety. The impression at this time was that the child had bronchopneumonia, rachitis, and malnutrition.

February 1, 1923: No temperature. Persistent, non-productive cough. Child looks toxic. Dyspnea still present and chest presents a moderate amount of musical and scattered, coarse, indeterminate râles. The impression at this time was the same as at the first, with the addition of a questionable diagnosis of asthma.

February 4th to 6th: The same physical signs with a continuous presentation of asthmatic breathing, the temperature remaining of a low-grade type. Our impression at this time was that we were dealing probably with an enlargement of the tracheobronchial lymph-nodes, which were probably producing enough pressure on the large bronchi to account for the persistence of asthmatic breathing which had been observed, now, for seven days.

At this time an intracutaneous Von Pirquet in a 1:1000 dilution was done and an x-ray ordered. At this examination a marked enlargement of the glands was evident in the left inguinal region. They were shotty and adherent to the skin, making us feel that we were dealing with tuberculous glands in this region, and in view of our impression that the asthmatic breathing was due to an enlargement of the tracheobronchial lymph-glands, an x-ray of the lungs and of the inguinal glands was ordered and a biopsy of the inguinal glands taken for histologic examination.

February 7th: x-Ray report (Fig. 156) gives the impression

of a subacute pulmonary tuberculosis with, however, a large degree of calcified nodes and particularly a great enlargement of the glands in the hilus and tracheal regions. There also appears to be a slow, proceeding tuberculous involvement of the lung parenchyma. x-Ray (Fig. 157) examination of the inguinal region presents calcified glands which suggest tuberculosis.

February 9th: There is dulness on percussion posteriorly over both lungs extending down to about the fifth rib. Dry

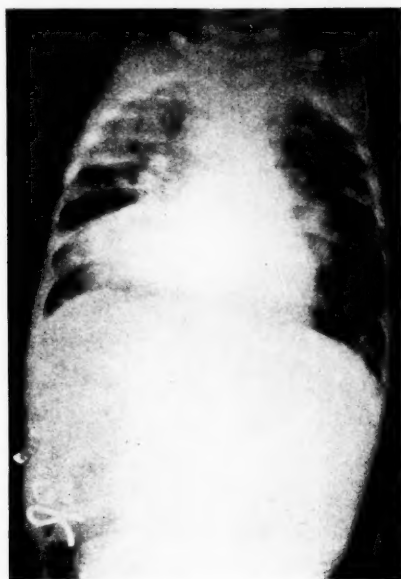


Fig. 156.—Case II: L. J., February 7, 1923.

râles audible in this region, while throughout both lungs are heard sibilant and sonorous râles.

February 13th: The patient is growing progressively worse. The signs of consolidation are spreading. Sibilant and sonorous râles (asthmatic breathing) still present.

February 17th: Child continuing to lose ground. Weight rapidly decreasing. Asthmatic breathing still present.

February 18th: Histopathologic report of the removed inguinal gland is that of tuberculous adenitis. Child continuing on downward grade with an antemortem rise in temperature. Six P. M. child ceased breathing.

Autopsy.—February 19, 1923: Body that of a colored male child, one year old, markedly emaciated.

Fontanel wide open. No dentition.

Mid-incision presents practically no subcutaneous fat. No fluid in peritoneal cavity. Peritoneum and great omentum



Fig. 157.—Case II: L. J., February 7, 1923.

studded with small white nodular masses appearing to be miliary tubercles.

Breast-plate shows no adhesions to the lungs. Both lungs present hard, nodular areas which on section are yellowish white in color, firm in consistency. Some, however, are caseous, while others present varying degrees of calcification. The bronchial lymph-nodes are enlarged and hard. There is generalized miliary tuberculosis and signs of tuberculous bronchopneumonia.

The heart is without evident lesions. The liver presents a normal appearance except that on section numerous small whitish areas (tubercles) may be seen. Gastro-intestinal tract is without evident lesions. The spleen on section presents numerous whitish areas similar to those seen in the other organs. Kidneys apparently normal. Bladder normal. Inguinal glands calcified. Brain normal, section of bones shows evidence of rickets.

Diagnosis.—Tuberculous bronchopneumonia, miliary tuberculosis (generalized). Tuberculous bronchial lymph-nodes.

Summary of Case II.—A colored, male infant, one year of age, on whom no history of tuberculous exposure was obtained, was admitted to the wards suffering from a marked respiratory condition. The striking feature of the case was that in addition to evidence of pulmonary tuberculosis there was an asthmatic breathing that persisted throughout the child's stay in the hospital, viz., over a period of eighteen days. If there were remissions of this asthmatic breathing they were temporary, because at all visits of the interns, or those of us on the visiting staff, asthmatic breathing was always elicited. In view of our experience with the former case several years before (Case I), we made a diagnosis of tuberculous bronchial lymph-nodes producing pressure on the bronchial tubes. This case also gave a strongly positive Von Pirquet, a tuberculous pathology of an inguinal lymph-node, and presented an x-ray picture which indicated an enlargement of the glands that was not obtained in the first case. Autopsy, as in the former case, corroborated the clinical findings.

In the cases following no autopsy records were obtainable and they are merely summarized.

Case III.—L. Z., male, white, was first seen at the Manhattan Maternity Hospital, November 10, 1921, at six weeks of age. He was admitted to the clinic for general care. This child had a definite history of exposure to tuberculosis through his father. At five months of age the child developed skin tuberculides and presented a positive Von Pirquet. No x-ray was obtained.

The child was observed for several weeks after this and presented, among other signs, definite wheezing râles in the lungs. He was transferred to a hospital and the information obtained from this hospital was that he succumbed to pulmonary tuberculosis shortly after admission. An autopsy was done which showed pulmonary tuberculosis, but we have been unable to procure the records.

Case IV.—R. K., male, white, admitted to the ward of City Hospital, June 23, 1924, as a general feeding case. For two



Fig. 158.—Case IV: R. K., August 8, 1924.

months after admission he presented signs that were suggestive of pulmonary tuberculosis. When the child was five months of age, in addition to fine crackling râles at each hilus and dulness at the apices, he developed sibilant and sonorous râles (asthmatic breathing). An intracutaneous Von Pirquet test made at this time was strongly positive. During the next two months

the child continued to have an almost unremitting asthmatic breathing and in view of our former experience we gave a fatal prognosis. The child, however, was given antituberculous, hygienic treatment and after two months the asthmatic breathing gradually subsided. The child at this time began to gain in weight and developed into normal infancy. At various times during subsequent observations he had recovered uneventfully from bilateral otitis media, varicella, and measles. Four months



Fig. 159.—Case IV: R. K., January 8, 1925.

later the asthmatic breathing could occasionally be heard, but for the most part it was absent at the various examinations. The Von Pirquet was again shown to be positive. The child was observed for one year and three months after his entrance into the hospital, and for the last six months gave no further evidence of asthmatic breathing, which we felt, in view of the positive Von Pirquet and the continuance of the signs, had been due to the pressure of the bronchial lymph-nodes.

Many x-rays of the lungs of this child were taken throughout the course of his asthmatic breathing in an effort to find further evidence for our diagnosis, but with the exception of moderate infiltration of the lungs, and, latterly, calcification of some of the lymph-nodes, the x-rays were of little value. (See Figs. 158, 159, which are two of the many taken.)

GENERAL DISCUSSION

This study has indicated that fundamentally we are here dealing with a symptom-complex which simulates what we regard as bronchial asthma. It is evident, however, after careful analysis of our findings, that we could not possibly make a diagnosis of bronchial asthma unless we were to regard the signs as indicative of a superimposition of a bronchial asthma upon tuberculosis. There is one striking point that militates against strict bronchial asthma, namely, that even though the signs are typical, the temperature of low grade, and occasional relief obtained from adrenalin injection, there is complete absence of probably the most characteristic element in asthma, namely, paroxysms. The asthmatic breathing in all of the above cases was continuous in type and entirely devoid of paroxysms.

Lapage and Adams,¹ in a study of asthma in children, feel that occasionally there are evidences of intrathoracic pressure, giving asthmatic signs. They cite the case of a child who suddenly coughed up large pieces of débris from a calcareous gland. This child became better and his asthmatic attacks subsided. Charles² reports the case of a young man suffering from asthma, which he shows to be the result of pressure. Throughout the young man's life he had been subject at intervals to typical asthmatic attacks which seemed to have all the earmarks of a typical bronchial asthma. At one time he went on a visit to Cornwall, during which time he was free from attacks, and it was thought that the climate had all to do with it. The patient finally noticed an enlargement of the thyroid gland, which appeared just behind the right clavicle, the asthmatic attacks at this time becoming more frequent. An x-ray was taken, which showed a definite shadow in the mediastinum on the right side,

bending the trachea over to the left. The diagnosis of an intrathoracic tumor was made and the tumor successfully removed by operation. At operation old hemorrhages were found surrounding the tumor. It was thought that after exertion the pressure due to these hemorrhages had become increased and the attacks had then occurred. The patient was observed for many months after the operation, but had no further attacks. Microscopic examination showed the tumor to be a unilocular colloidal cyst, adenoma.

Hanzlik and Karsner,³ in their work on anaphylactoid phenomena in guinea-pigs, present a theory which they call "passive broncho-constriction," meaning a narrowing of the bronchial tube due to outside pressure (thrombosed pulmonary vessels in their instance) as opposed to active broncho-constriction which is a direct contraction of the smooth muscles of the bronchi and bronchioles (really a spasm) and which is evidently the condition found in asthma.

The striking evidence of a tumor pressure on the bronchi presented by Charles and the experimental evidence presented by Hanzlik and Karsner we feel bear out our viewpoint in the cases we have presented, namely, that we are dealing with asthmatic signs due to pressure on the bronchi, which is a passive broncho-constriction and not the active broncho-constriction that is present in true bronchial asthma.

In the second case (L. J.) there is radiographic evidence of enlarged bronchial lymph-nodes, and though the autopsy findings were just as characteristic in the first case (J. W.), the radiographic evidence was not present. The fourth case (R. K.) showed no x-ray findings that were helpful. x-Ray, therefore, does not give positive findings in all cases.

If we are correct in our impression, cases of this type, it appears, need not be fatal unless the tuberculosis becomes too widespread. The enlarged tuberculous glands may subside and calcify, as was indicated in Case IV.

A fifth case was admitted to the City Hospital, that we placed in this group because of the striking signs of continuous asthmatic breathing, but our diagnosis was incorrect. This

case (N. G.), a colored infant a little more than one year old, throughout his stay of seven months in the hospital did well. At no time did he present evidence of tuberculosis that was conclusive. The Von Pirquets were persistently negative and the x -rays of little help. This infant was markedly rachitic, with marked thoracic deformity.

The asthmatoïd breathing that is found when a foreign body such as a peanut enters the bronchus (as so nicely shown by Chevalier Jackson), the evanescent asthmatic breathing heard in whooping-cough, bronchopneumonia, bronchitis, marked nasal obstruction, and cases of severe rickets (as above, N. G.) may probably be explained as another form of "passive bronchoconstriction" not due to outside pressure, but to an increased turgescence and an increased amount of mucus in the bronchi, producing a narrowing of the lumina.

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CLINIC OF DR. SEYMOUR FISKE

MIDTOWN HOSPITAL

DIABETES MELLITUS IN RELATION TO GASTRO-INTESTINAL DISEASE

IN the routine examination of patients in the clinic of a hospital the number of patients suffering from diabetes mellitus brought to the attention of the physician in charge of the gastro-intestinal clinic is relatively small. This may be accounted for in several ways. First, because a diabetic's symptoms do not usually involve the gastro-intestinal tract, the patients are more apt to consult their physician because of their inordinate appetite, or polydipsia, or increasing weakness, which at once gives a clue to the diagnosis. Second, in the diagnosis of consulting physicians, both in private practice and in the clinic, a urinalysis is becoming an increasingly routine procedure, especially the tests for albumin and sugar, the presence of which in the urine immediately indicates the diabetic condition or reveals the presence of a glycosuria. Third, due to the wide-spread advertisements of the various pharmaceutical houses the laity are gradually accumulating a general knowledge of diabetes, its cause, and the newer method of insulin treatment.

Within the last six months in the gastro-intestinal clinic of the Midtown Hospital, New York City, only 1 case with a true diabetic condition came to our attention out of 66 admissions to our department for stomach complaints.

This condition, furthermore, was not brought out in the history, but was discovered in the routine urine examination, which is made upon all of our patients.

The gastro-intestinal symptoms which are apt to appear late in any true case of diabetes, owing to the nature of the disease,

include general weakness and lassitude, excessive gas and constipation. These symptoms, as stated above, usually appear late in the onset of the disease because true diabetes is a disease of the pancreas, yet of a limited part of the pancreas, namely, the islands of Langerhans. Hence, anatomically, the secretions of the pancreas which enter the gastro-intestinal tract are not directly affected in diabetes mellitus. Even though the islands of Langerhans are undergoing disease changes, the digestive functions of the pancreas may continue practically normal. These functions, then, become involved only when the organism as a whole has begun to break down under the strain of improper catabolism of the body glucose, as it accumulates in increasing amounts in the blood-stream. In other words, although diabetes is a disease in which the primary pathology is located in one of the accessory organs of digestion—and a very important one, too—its effects are not apt to be manifested upon the gastro-intestinal tract until the digestive functions of the organism fail, simultaneously with the failure of other bodily mechanisms, due to overloading of the body metabolism in its failure to utilize its glucose normally.

The symptoms arising from this gastro-intestinal failure are a general sluggishness of intestinal motility, giving rise to the motor etiology of attending constipation. The food-stuffs are not properly digested as they pass through the intestinal canal and thus a vicious circle prepares the way for gaseous distention of the stomach and the colon. Because the intestine does not absorb its food supply properly, weakness is brought about by the inability of the organism to digest and assimilate its fuel—namely, food.

In the differential diagnosis of diabetes mellitus as it relates to gastro-intestinal disturbances, there are two points of view, namely, that of the gastro-intestinal tract and its function, and that of pancreatic function. The patient's history is usually of paramount importance in eliciting the true relationship of the intestinal symptoms to some possible underlying diabetic etiology. The additional scientific tests upon which an accurate differential diagnosis may be based are, of course, the urinalysis,

which ought to be of a twenty-four-hour specimen of urine, and a quantitative sugar determination where sugar is present. In the presence of sugar in the urine a blood-sugar examination should be carried out upon a fasting stomach. In this connection, it is also worth while in a differential way to do a complete blood chemistry, as in this way additional information is given with regard to renal and hepatic functions serving to rule out the type of glycosuria which comes from moderate renal insufficiency, or association with an essential hypertension. Blood-pressure examinations are likewise of value in ruling out the type of glycosuria due to an essential hypertension. In most diabetic conditions complicating gastro-intestinal disturbances the blood-pressure is low. Gastric analysis is, of course, a test routinely made upon patients suffering from gastro-intestinal complaints. Its particular value in the relationship under discussion is as an aid in treatment, for there may be some true gastro-intestinal pathology such as a hypo- or hyperacidity in these cases. Just which condition predominates is apt to depend upon the duration of the diabetic condition as well as upon the nature of any additional gastro-intestinal pathology.

TREATMENT

In the treatment of gastro-intestinal symptoms complicating or incidental to a true diabetic disease process, there are two points of view. One must treat the diabetes in accordance with the latest knowledge of the scientific treatment of diabetes by the combined utilization of insulin and adequate diet regulation. One must also treat the intestinal symptoms. The treatment may be modified to meet the demands upon the bodily metabolism due to the impaired utilization of carbohydrates. Most patients who have stomach symptoms starve themselves or put themselves upon peculiar and unusual diets which they obtain from their friends without regard as to whether they have any actual physiologic or scientific basis. In the writer's opinion, it is wisest, therefore, to treat these intestinal symptoms first along the lines of general intestinal dietary therapeutics with, however, due regard for the patient's ability to utilize

carbohydrates. This ability should be determined after careful scientific studies have been made and the patient kept upon the regulation basal diets for diabetics. If, on the other hand, the urinalysis and blood chemistry indicate that the diabetic condition is very far advanced, the diabetes should be treated with proper dosages of insulin and with very strict diet control.

A patient with more than 2 per cent. sugar in the urine should preferably be hospitalized for a week or ten days, until the various studies required may be carried out and the patient's diet stabilized and regulated in order to obtain a minimum tolerance diet and a minimum of gastro-intestinal disturbance. It is only by controlling the patient in some such fashion and by treating each disease entity as a separate condition that one may arrive at a true valuation of the possible predominance of either the gastro-intestinal or the pancreatic pathology.

When the diet regulation has succeeded in alleviating intestinal symptoms, and when a maximum tolerance diet has been worked out, with sugar-free urine, steps may be taken to regulate the amount of insulin compatible with the increasing dietary freedom. Naturally, a patient must be instructed in the choice of his diet articles and be given instruction regarding the carbohydrate contents of food-stuffs. If possible, he should be taught the sugar-test for his urine, which should be made at least once a week. With regard to the intestinal tract normal elimination of the contents of the large bowel and a normal functioning of the entire intestinal canal corresponding with the increased intake of food should be aimed at. When a patient is handled along such lines it is often possible to eliminate either one or the other of these conditions. If the intestinal symptoms clear up, the patient may then be transferred to a diabetic clinic for further care, or if the diabetes is easily cleared up then the gastro-intestinal department may continue the care of the patient in order to avoid a further occurrence of intestinal symptoms. In view of the dietary restrictions usually employed in the treatment of diabetes, active medication of the intestinal tract is contraindicated. Practically the only treatment for the stomach and intestine available is a means of overcoming a tendency to

constipation, such as the use of cleansing enemas or the relief of hyperacidity of the stomach by means of sodium bicarbonate. Diarrheas are not apt to occur. If they do, and should they be in any way bothersome, they may easily be controlled by bismuth subgallate, gr. v, taken every three hours. A plain mineral oil as an intestinal lubricant is probably the best laxative and should be taken twice a day in tablespoonful doses. The gaseous distention complained of may be relieved by hot packs to the abdomen or by simply cleansing irrigations of the colon. It is occasionally advisable, after the cleansing injection, to introduce a quart of warm water containing ten drops of iodine. This will sometimes stimulate the expulsion of gas when ordinary soap suds will not. With proper attention to the food intake, and as the digestive processes improve in accordance with the improved ability of the body to utilize its glucose the gaseous condition of the intestinal tract is not apt to recur, or, if so, only sporadically.

In the future management of these patients little difficulty ought to be experienced once one has worked out the predominating condition, that is to say, either diabetic or intestinal. As already noted, usually one or the other condition may be eliminated in the course of a short time and the patient then be carried on from the point of view of only a single disease process.

There are, of course, complicating factors in the handling of these patients. These are the factors incident to the diabetic process in the pancreas. To name these in the order of their influence on diabetic mortality as determined by the statistics collected by Dr. Reginald Fitz at the Peter Bent Brigham Hospital, Boston, during the ten years prior to 1923, they are diabetic coma and acidosis, sepsis, cardiovascular disease, and pulmonary tuberculosis. Obviously, the occurrence of any of these complications increases the gravity of the condition and points the way to the more immediate treatment of the underlying diabetic condition. Two other complications occurring to the writer as being of paramount importance, though not perhaps as forbidding in their bearing upon prognosis, are the nervous

disorders causing the neuritis and neuralgia often accompanying diabetes, and the secondary blood disturbances and bone-marrow changes causing secondary anemias and impoverished blood pabulum. The presence of any of these complications would indicate more strongly than ever to the physician either in private practice or in his clinic work the imperative necessity for proper hospitalization of the patient.

The breaking down of the integrity of the gastro-intestinal tract presents another group of complicating factors. These may involve not only digestive disturbances but also the motor function and power of the intestine, leading to intestinal atony or intestinal spasm. As a result of increased spasticity there are accompanying abdominal cramps and pains. As a result of the atony there come anatomic ptoses of the stomach and the colon, leading to pain in the back, constipation, and intestinal poisoning. Hyperacidity is more apt to be the rule, leading to spasm, epigastric pain, regurgitation of food, and vomiting.

By way of illustration of the above remarks the following case is presented.

D. M., female, colored, married twenty-one years; husband living and well. No children and no miscarriages.

The patient was admitted on June 19, 1925. Her chief complaint was gas. Her present illness indicated that she had never had any vomiting, but during the past two years had been troubled with "gas on the stomach all the time." There was anorexia, also a complaint of a dry and very coated tongue. Following the belching of gas there would often be sour eructations of food. The patient's habits showed that she was very constipated, slept well at night, drank plenty of water. She gave no history of polydipsia. She drank three cups of tea a day and no coffee. She was an occasional user of Carter's liver pills. She had sustained no injuries. In 1917 she had had a pelvic tumor removed at Bellevue Hospital, New York City. She complained of cataracts of both eyes. The patient's medical history was essentially negative except that she always suffered from constipation and frontal occipital headaches. Her menses have been and still are normal in occurrence.

Physical examination revealed a very undernourished middle-aged woman, colored, weighing approximately 100 pounds, with anxious facies. She had bilateral cataracts of both eyes, not yet operable. The pupils reacted promptly to light and accommodation. Throat clean. Tonsils medium in size, not diseased. Teeth, upper, false plate; lower, present in satisfactory condition. Gums not infected. No thyroid enlargement and no other adenopathy. Heart regular, rapid, sounds strong and of good quality. No murmurs. Pulse 90. Blood-pressure 120/80. Lungs clear throughout. Abdomen slightly distended and tympanitic throughout. No palpable organs and no points of acute tenderness. Extremities negative. Knee-jerks present, active and equal. Skin clean.

The tentative diagnosis made on this patient on admission was that of chronic constipation with hyperacidity. The routine urinalysis done on June 22d, three days after admission into the gastro-intestinal division, revealed a faintly acid reaction, specific gravity 1.030, a trace of albumin, 0.015 per cent. Sugar present to the extent of 3.33 per cent. Urea normal, 1.529 per cent. There was an excess of total solids amounting to 6.990 per cent. Microscopic examination showed no pus, blood, or bacteria. There were a few cylindroids, ten hyaline casts, a small number of leukocytes, no crystals, and a moderate number of squamous epithelial cells.

A gastric extraction was made on this patient one morning, although she had not followed instructions about meals, ninety minutes after she had eaten Cream of Wheat and a glass of milk. About 100 c.c. of gastric contents was obtained, not of a particularly sour odor. This large amount of food in the stomach after so long a period would indicate some gastric retention in this patient's condition probably due to a gastroparesis. The report of the gastric analysis follows: no lactic acid, no bile, a large number of starch cells, a large number of fat globules, a trace of mucus, small number of squamous epithelial cells, and a large amount of disintegrated starch cells. An examination of the urine at this time revealed 2.4 per cent. sugar.

Upon receiving the report of the urine, we placed the patient

upon a laxative diet with restricted carbohydrate intake. Squibb's mineral oil, a tablespoonful twice a day, was given to help lubricate the intestine, and an alkaline powder of equal parts of magnesium carbonate, sodium bicarbonate, and bismuth subcarbonate was prescribed, a teaspoonful in water one hour after eating, to allay any gastric acidity and to alleviate the flatulence. Squibb's insulin injections were resorted to, being increased rapidly to 20 units three times a week. These were given just before the patient ate lunch. They could not be given oftener because the patient could come into the clinic only three days of the week.

On the above treatment the patient showed rapid improvement with relief of the gaseous distention. The bowels commenced functioning daily and the patient stated that in the course of two or three weeks her family noticed a marked improvement in her general appearance and in her mental reaction to her environment. Even under the handicaps present in this case the urine, which has been examined regularly once a week, has shown a marked improvement, the last examination on August 7, 1925 showing the following: Clear, moderately acid. Specific gravity 1.020. Albumin, none. Sugar 1.98 per cent. Total solids 4.66 per cent. Nine hyaline casts, a few leukocytes, and no crystals.

Due to the fact that the patient's gastro-intestinal symptoms improved so rapidly she was considered as falling into the group of true diabetes and was given over to the prescribed treatment. During eight weeks the patient's weight fluctuated somewhat, but reached a maximum of 110 pounds on August 1st. On August 12th she had lost to $107\frac{1}{2}$ pounds, but this she felt might be due to the fact that she had not been eating so much and had also been taking sugar against orders and had, in addition, been worrying about her eyes, for which operative intervention is planned as soon as her general condition is built up sufficiently.

CONCLUSIONS

In summarizing the account presented it may be noted:

First, that the influence of diabetes mellitus upon the gastro-intestinal tract is apt to appear late in the course of events, due to the etiology of the true diabetes and to the insidiousness of the attack upon the intestinal functions.

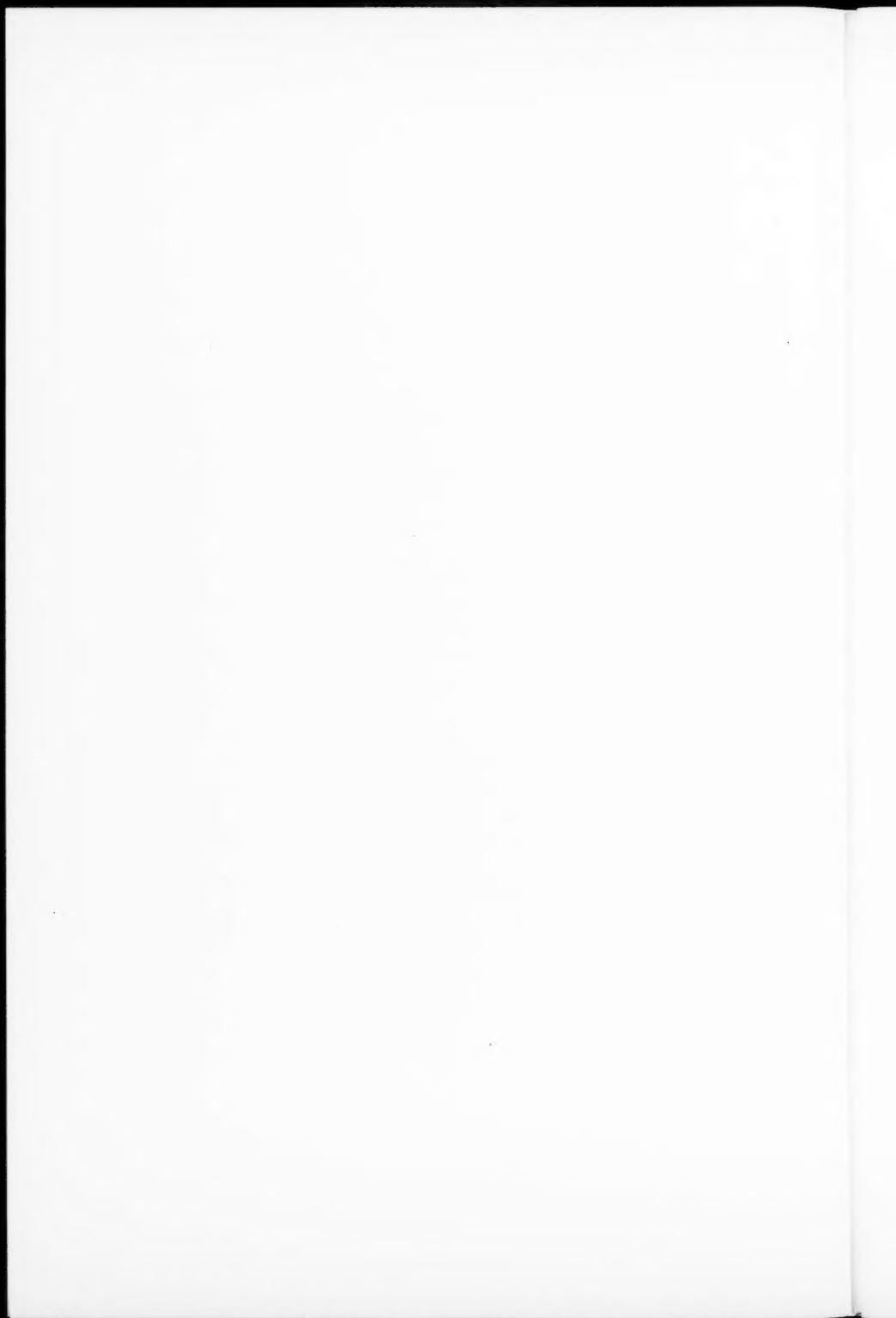
Second, a routine urinalysis is the most important single differential diagnostic test.

Third, the management of such a condition of double pathology is referable chiefly to careful dietary control selected with two points in mind: (a) aiding the body metabolism in its available and potential assimilative processes, *i. e.*, improvement of constipation, and (b) the gradual recovery of the organism's metabolism to a point of maximum carbohydrate tolerance and utilization.

Fourth, supportive chemical treatment with insulin injections and other indicated therapeutic agents to improve abnormal conditions in the intestinal tract itself.

Fifth, careful scientific study and investigation of the pathology manifested by both disease processes to determine, if possible, the predominant or primary etiologic process.

Sixth, adequate control, guidance, and instruction of the patient with regard to his future health.



CLINIC OF DR. JOSEPH M. MARCUS

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CARDIOSPASM

LESIONS of the esophagus are more frequent than is generally supposed; and next in frequency to cancer of the esophagus is cardiospasm, that is, spasm of the musculature of the cardia or epicardia causing a partial or complete obstruction. This obstruction is usually associated with a compensatory dilatation of the esophagus above the point of the disease.

Purtan in 1821 reported the first case of cardiospasm. Zenker and Von Ziemsen in 1878 compiled 17 cases from the literature. Recently the subject has been elaborated by Einhorn, Sippy, Smithies, Plummer, Vinson, and others.

ETIOLOGY

As yet there has been no satisfactory explanation as to the etiology of the disease. Among the theories suggested are that the case may be primary spasm at the cardia or that it may be atony of the musculature of the esophageal tube. It has also been suggested that the lesion is of the irritative type, involving the vagus nerve or an involution of the esophagus at the cardia. Kinking of the esophagus at the hiatus esophagi has also been suggested. Chevalier Jackson¹ has demonstrated that in many instances cardiospasm is in reality a hiatal esophagismus or phrenospasm. Liebault² says that the anatomic basis for this fact is furnished by the observations of himself and Rouget. They found the existence of special muscle bundles connecting the esophagus with the crura of the diaphragm at the level of the hiatus.

Since many patients suffering with cardiospasm also suffer from hay-fever or asthma, it has been suggested that there is a

probable relationship to some form of protein sensitivity or allergy.

Vinson³ classifies 415 patients seen at the Mayo Clinic. The age of the patients vary from five to eighty-three years; one-third were in the third decade of life. Two hundred and forty-six patients (59.3 per cent.) were males and 169 (40.7 per cent.) were females. Smithies,⁴ however, found 25 females to 22 males in his group of 47 cases.

SYMPTOMS

The symptoms may be mild, with just a slight feeling of sub-sternal obstruction upon the passage of food. There may or may not be pain, and roentgenographic evidence may be lacking in the early stages.

In the history, difficulty in swallowing, dysphagia, a localised feeling of pressure in the course of the tube, or regurgitation of food makes a special examination of the function of the esophagus necessary. Dysphagia may set in suddenly or may begin insidiously and gradually increase. In esophageal stenosis, especially, the patients state that they have been compelled to use foods of ever softer consistency until finally only fluids could be swallowed. They either regurgitate food immediately or they feel that it must remain in the esophagus to be regurgitated later, perhaps in a decomposed, foul-smelling state. In these patients emaciation comes quickly. Where there is great variation in the ability to swallow, a cardiospasm or a diverticulum of the esophagus should be suspected. Pain on swallowing may be sharply localized to one spot on the anterior chest wall or the pain may be diffused throughout the whole length of the gullet.

The duration of the symptoms in Vinson's group was from two months to forty-five years. The average duration was seven years. The onset was sudden in 67 patients.

The symptoms may vary according to the stage and degree of dilatation. In the first stage one sees incomplete obstruction; second, regurgitation of food immediately after meals takes place; and finally, the regurgitation may be delayed for hours

or even days. The most common symptom is dysphagia which may vary from slight to complete inability to swallow. Fluids are likely to create discomfort as well as solids. Raw fruit, cold water, and popcorn give the most trouble (Vinson). Some patients acquire a knack of forcing food into the stomach by drinking several glasses of water after a meal, thereby causing a relaxation of the cardiospasm.

Many of the patients regurgitate mucus and food at night. One never finds gastric contents in this regurgitated esophageal material.

Respiratory symptoms, such as cough and dyspnea after eating, are common and are most likely caused by pressure of the dilated esophagus upon the bronchi. Hiccup occurs in some cases. The pain of gall-bladder colic and angina pectoris may simulate the pain of cardiospasm.

DIAGNOSIS

If one listens near the xiphoid cartilage or along the lower dorsal vertebræ, after a patient has swallowed a mouthful of water, two murmurs may be audible; a primary, so-called squirting murmur, and soon after a secondary, so-called squeezing murmur. Usually, only one of these murmurs is present in the same person, though in exceptional cases, both murmurs may be audible. Meltzer⁵ regards a distinct squirting after a single act of swallowing an evidence of insufficiency of the cardia. A total absence of squeezing murmurs may indicate stenosis of the cardia.

Deglutition is a complex reflex, which may be initiated voluntarily, but is, as a rule, independent of the will. When studying disturbances of deglutition the student should refresh his memory of the normal physiology. Most careful studies were made early by Kronecker and Meltzer.⁶ Recently, with the aid of the roentgenograph, the physiology of deglutition has become better understood (Cannon⁷). Fluoroscopy shows that two periods can be distinguished: (1) a buccopharyngeal, (2) and esophageal. The former lasts less than one and a half seconds, the

latter four to seven seconds. The two periods have been compared to the atrial and the ventricular activity of the heart.

The three important methods of examining the esophagus are: (1) The passage of esophageal bougies; (2) Roentgen-ray examinations of the esophagus, and (3) esophagoscopy. Of these three methods, the second is probably the one from which we obtain most help.

INSTRUMENTATION

Before passing a sound, or a bougie, to investigate the nature of the difficulty in swallowing, the heart and large vessels should be carefully examined, and if an aneurysm be found or even be suspected to exist, no bougie should be passed. Fatal hemorrhage has more than once occurred from rupture of an aneurysm by an esophageal bougie.

Other contraindications are outspoken circulatory insufficiency, recent vomiting of blood, acute mediastinitis, and severe cachexias. Strong force should never be used in passing a bougie, for if there be an ulcer, or if the wall of the gullet be thinned by an abscess in the neighborhood, perforation may easily occur.

It is advisable to begin by passing an ordinary Ewald stomach-tube in the usual way. If this meets with resistance at any point, recourse to a firmer instrument (sound or bougie) is necessary.

For sounding the esophagus, the whalebone sounds with olive-shaped tips or mushroom-shaped tips, of varying sizes, are most often used. Gum-elastic silk woven bougies are also employed. Recently, the use of a silk thread previously swallowed as a guide to the sound has proved very useful. The sound is previously lubricated with a little glycerin or with vaselin. Old sounds are to be avoided if at all rough, as they easily injure the mucous membrane.

The patient should sit on a stool, the body bent slightly forward, and the head a little backward; a basin should be held in one hand to be used in case of vomiting. He is told to hold the mouth wide open, to breathe quietly and regularly, and to avoid gagging. He should be assured that the examination is painless and harmless. The physician stands in front of or on

one side of the patient. With the forefinger of his left hand he makes a strong pressure downward and forward upon the tongue, thus drawing the epiglottis and the cricoid cartilage forward and widening the opening of the esophagus. The bougie, held

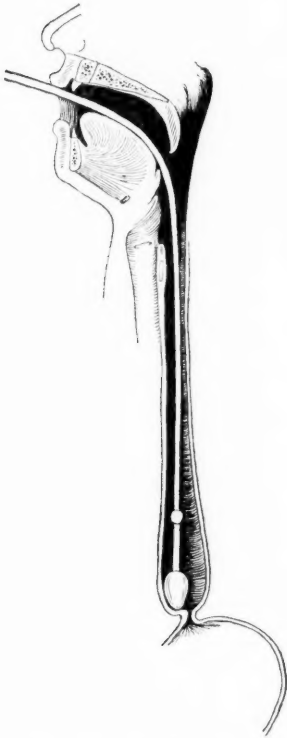


Fig. 160.—Bougie with olivary tip in dilated esophagus, showing danger of perforation.

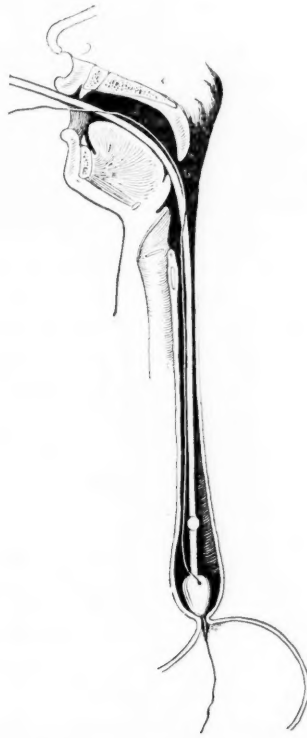


Fig. 161.—Bougie with olivary tip threaded on string to guide instrument through cardiac orifice.

like a pen in the right hand, is now passed straight backward in the middle line of the pharynx; the upper end of the bougie is then elevated and the tip gently slid into the esophagus. Care must be taken to avoid (1) the sinus pyriformis on each

side of the larynx, (2) entrance of the sound into the larynx, which, of course, would cause dyspnea and coughing. Once in the esophagus, the bougie is slowly pressed downward until it either reaches the stomach or meets with resistance. Occasionally a resistance is encountered that is due to temporary spasm of the wall of the esophagus. When this occurs, one waits a few moments until the spasm passes off and then proceeds with the further passage of the bougie.

If resistance is met with, its exact position, degree, and nature should be investigated. First, its distance from the incisor teeth is measured, and the measurement repeated on the different days to see if the resistance is constantly at the same level. The caliber of a narrowed esophagus is measured by finding the sound (beginning with the largest and using successively a series of smaller ones) that just passes through without the exertion of any considerable force. The length of the narrowing is found by passing an olive-tipped sound through to the stomach and again withdrawing it, noting the distance from the incisor teeth at which the resistance is first felt on withdrawal. The difference of the distances of the two resistances from the incisor teeth indicates the length of the narrowed portion of the tube.

TREATMENT

Occasionally belladonna or atropin administered to the physiologic limit may relieve cardiospasm in psychoneurotic patients. As a rule, however, medication is quite unsatisfactory.

Russell has devised a rubber bag, to be swallowed and filled in the cardia with air or water. However, water is preferable as it is less dangerous and more easily controlled, and it is not as compressible as air. The degree of pressure in dilating depends upon the dilatation of the esophagus above the spasm. With a small dilatation the pressure should be equal to a column of water ranging from 16 to 22 feet. When the spasm is more marked the pressure should be increased to 24 to 28 feet. This is obtained by using a hydrostatic dilator after the suggestion of Plummer,⁸ as shown in accompanying figures.

There should be a gradual increase to the desired hydrostatic pressure. This pressure should be kept up from two to five minutes, then the dilator should be emptied and withdrawn.



Fig. 162.—Dilator bag with olivary tip and guiding string.

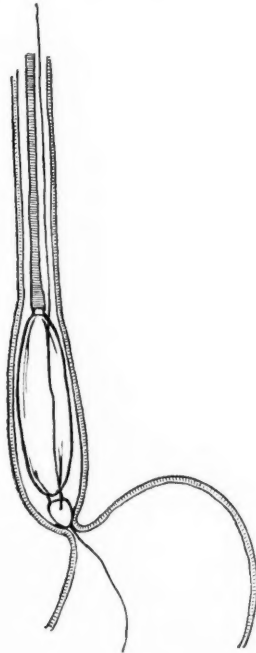


Fig. 163.—Olivary tip and string guiding dilator through cardiac orifice.

The pain arising from dilatation may occur immediately or may be delayed for twenty-four to thirty-six hours.

Complications arising from this treatment are rare. There have been moderate hemorrhages from the esophagus. There

also has been pleurisy with effusion. Fatalities, though rare, have been reported.

The immediate results are remarkable, being associated with complete loss of symptoms and gain of weight. The dysphagia recurs in about 25 per cent. of the cases in six months.

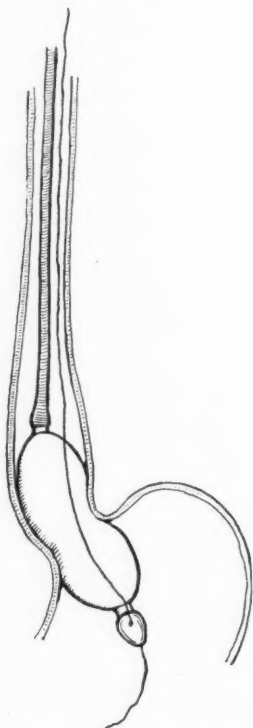


Fig. 164.—Expanded bag dilating cardiospasm.

A few cases are not completely cured. The majority, however, have complete relief if the treatments are continued.

It is of interest to note that even though there may be complete relief of the symptoms of cardiospasm after hydrostatic dilatation of the cardia, the roentgenographic findings of the esophagus remain unchanged.

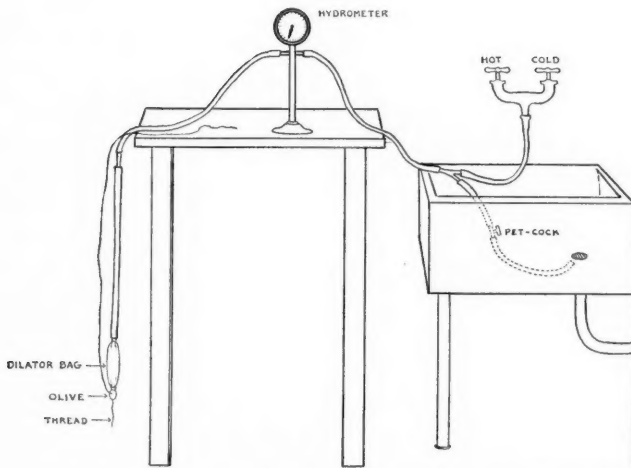


Fig. 165.—Assembled apparatus showing hot and cold water supply to regulate the temperature of the dilator, meter to indicate and pet-cock to regulate the pressure of water in dilator bag.

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